Personality Correlates of Adherence to Antiretroviral Therapy in HIV Infection

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Declaration

I hereby declare that the work enclosed herein is my own except where otherwise stated.

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Abstract

Ability and willingness by HIV-positive individuals to maintain a high level of adherence with complex antiretroviral treatment is critical to the success of Highly Active Antiretroviral Therapy (HAART).

A sample of HIV-positive individuals, accessing antiretroviral therapy from Lothian based services, was assessed in order to determine if associations existed between personality characteristics and level of adherence to treatment regimens. Physiological and self-report measures of adherence were consulted. Personality and coping style were evaluated using standardised assessments. Non-parametric statistical tests were applied during the analysis.

Results indicated that there was evidence for an association between level of treatment adherence and two personality styles, two coping styles and two indicators of treatment prognosis.

1 Introduction

When cases of AIDS were first diagnosed in 1979, and until quite recently, the disease was considered to carry an almost certainly debilitating, downward course leading to early death from opportunistic infections. Early medications used to treat AIDS-related diseases, such as AZT (or Zidovudine), could only temporarily suppress the levels of HIV responsible for immune compromise. Benefits were often only transient since circulating HIV remained in enormous quantities (termed *viral load*), and also because the virus has a rapid and error-prone replication cycle that allows it to quickly evolve resistance to any single antiretroviral medication. In 1996 the nature of HIV medical care, and the health outlook for patients, changed dramatically with the advent of treatment regimens that added a new class of antiretroviral medication (termed *protease inhibitors)* used in combination with other antiretrovirals.

Highly active antiretroviral therapy (HAART), usually a protease inhibitor combined with at least two other drugs, can suppress HIV viral load to undetectable levels, increase indicators of immune system functioning such as CD4 lymphocytes[1], improves clinical health, and decreases AIDS-related mortality (Carpenter et al., 1998). The success of HAART requires the continual suppression of HIV viral load to such low levels that the virus cannot replicate rapidly enough to develop medication resistance.

Early optimism regarding the widespread benefits of these medications is now tempered by evidence that a significant proportion of individuals do not achieve or sustain maximum reductions in viral load. Disease stage and previous antiretroviral treatment history does influence response to current HAART treatment. However, an especially critical determinant of treatment success is patient adherence. HAART

regimens require that patients take multiple doses every day of each medication in the combination. This can mean taking 20 or more pills a day, with each medication in the regimen carrying specific dose-spacing requirements.

Depending on the combination, different medications within a particular treatment regimen may need to be taken with food, without food, with water, or in temporal sequence relative to other drugs in the combination. In a recent drug trial, failure of patients to take even a *single* medication dose on 28 days during a 365-day clinical treatment course, was strongly associated with treatment failure (Montaner et al., 1998).

Helping patients achieve and maintain a successful response to HAART is very significant for reasons related to both the patient's own well-being and the public health. If adequate viral suppression is not achieved and sustained, the patient's HIV infection can become permanently resistant to most current antiretrovirals. Those who develop drug-resistant HIV can transmit these strains to others during high-risk activities. Because research on chronic illness other than AIDS has shown that patients have more difficulty adhering to complex regimens (Agras, 1989) or regimens that include multiple medications (Blackwell, 1992), HAART regimens are likely to prove especially difficult to adhere to. For medicine to bring about full benefits for patients and the wider society in HIV care, it is essential to identify factors that influence HIV treatment adherence and to then develop approaches to promote adherence.

[1] A CD4 lymphocyte is a small cell that is distributed by the bone marrow, but is developed in the thalamus of the brain. CD4 lymphocytes cause cellular immune responses. They are also referred to as CD4 cells, Helper T-Cells or simply T-Cells.

1.1 HIV and AIDS

The following sections provide a general introduction to the main concepts behind HIV/AIDS. This will include an analysis of the background to the HIV epidemic, theories of causation, transmission of HIV, stages of HIV infection, and various other issues which are important to consider in any introduction to HIV/AIDS as an area of research.

1.1.1 Introduction to HIV/AIDS and issues of treatment

HIV stands for Human Immunodeficiency Virus. It was originally isolated in Paris in May 1983 and belongs to a group of viruses called retroviruses. Viruses copy their genetic material into the genetic material of human cells. This means that infected cells stay infected for the rest of their lives. Through mechanisms, which are still not understood, HIV prevents the immune system from working properly. Normally, the body's immune system would fight off infection. HIV infects key cells (CD4 cells) which co-ordinate the immune system's fight against infection. Many are actually destroyed by being infected. Others, including CD4 cells, which are not themselves infected, no longer work properly. The human immune system is immensely complex and there are many ways in which it can be affected by a retrovirus such as HIV. It is not clear what role (if any) other factors - known as co-factors - may play in the development of immune damage. Although it is clear that HIV has a central role in the development of AIDS, there remain unanswered questions about some of the specific mechanisms by which it damages the immune system.

The definition of Acquired Immune Deficiency Syndrome (AIDS) has changed over the years as a result of an increasing appreciation of the wide spectrum of clinical manifestations of infection with HIV. Currently, AIDS is defined as an illness characterised by one or more indicator diseases. Both in the presence or absence of other causes of immune deficiency and with or without laboratory evidence of HIV, certain diseases when definitively diagnosed are indicative of AIDS.

1.1.2 Theories of origin of HIV

While discussion of the origins of HIV is interesting and potentially important scientific debate, it is necessary to separate origins from cause. For example, the identification of the origins of HIV in African primates does not explain the cause of the pandemic.

1.1.2.1 Types of retroviruses

HIV-1 and HIV-2 are just two members of a family of viruses called retroviruses. Other viruses in this group are known to infect:

- Humans, causing blood and nerve problems (HTLV-1)
- Cats (FIV, which causes an AIDS-like illness in some cat species but not others)
- Monkeys (a variety of viruses called SIV – Simian Immunodeficiency Virus – which causes an AIDS-like disease in some species of monkey)
- Sheep (a retrovirus which causes pneumonia).

1.1.2.2 The primate theory

HIV-1 is closely related to a version of SIV found in a species of chimpanzee. Researchers have discovered a virus in these chimpanzees that appears to be a 'mosaic' virus which combines elements of HIV with features of SIV. This virus is between 70%-90% identical to HIV-1. Known as SIVcpz, this virus does not appear to cause illness in the chimpanzee host. HIV-2 originated in the 'sooty mangabey' monkey. As with SIVcpz in chimpanzees, this virus does not cause illness in sooty mangabeys. Researchers believe that most African primates species have been infected with a sexually transmitted form of SIV for thousands of years and that these viruses no longer harm their hosts. However, when one type of SIV crosses into a different species, it does cause illness. This theory suggests that HIV-1 and HIV-2 may have been in the human population for anywhere between 25 and 100 years. It is thought that HIV successfully crossed the species barrier leading to the current HIV epidemic in humans. The hunting and consumption of monkeys and

apes by humans is thought to have led to HIV infection in humans. While it is likely that forms of SIV have been infecting humans for a long time, virus mutations may have led to the development of immunodeficiency viruses that were better able to cross the species barrier and sustain infections in humans.

1.1.2.3 The polio vaccine link

This theory claims that HIV was spread from chimpanzees to humans through an oral polio vaccine. The theory has been in circulation since the early 1990s. It is argued that a polio vaccine, administered in central Africa in the late 1950s, was cultured from primates infected with a version of SIV which subsequently infected humans. The appeal of this theory relies on timing; administration of the vaccine from 1957-1960 coincided with the first confirmed case of HIV infection in Africa. Independent analysis of the remaining stock of the vaccine has been conducted by a number of researchers who conclude that there is nothing in the results to support the theory that HIV was spread to humans via the polio virus clinical trials. They suggest that HIV has been infecting humans for much longer than 40 years. Other theorists have questioned this latest evidence and continue to support the polio vaccine theory.

Scientific investigation of origins may help to understand how to combat HIV most effectively. It is worth investigating populations who may have been exposed to HIV for many years, such as those in Africa, in terms of understanding the actual history of HIV, its virulence, and possible immunity to it.

1.1.3 Transmission of HIV

HIV has been isolated from semen, vaginal secretions, lymphocytes, cell-free plasma, cerebrospinal fluid, tears, saliva, urine and breast milk. However, not all these fluids transmit infection, as the concentration of virus in them may be far too low to be infectious. Particularly infectious are semen, blood (including menstrual blood) and possibly cervical secretions.

The main ways in which HIV is transmitted are:

- Through unprotected anal or vaginal sexual intercourse. This is the commonest mode of transmission of the virus throughout the world.
- Through blood to blood contact. This mainly happens through the sharing of injecting equipment among injecting drug users. In the past, before screening was introduced, this also occurred through blood transfusions or from infected blood products such as the Factor VIII used to treat haemophilia. Very rarely, infection can occur through occupational accidents amongst healthcare workers, such as needle-stick injuries or skin and mucosal exposure to infected blood or body fluids. Fortunately, follow-up studies of healthcare workers suffering percutaneous exposure to a known HIV seropositive patient indicate a transmission rate of 0.32%.
- Vertically, from an HIV-positive woman to her baby during the course of pregnancy (in utero), at birth, or during breast-feeding. The average risk of transmission during pregnancy is in the region of 10-15%, although it may be greater if the mother has a high viral load (the amount of HIV in her blood which indicates the rate at which the virus is reproducing in the body) or has developed AIDS.

The virus is not spread by casual or social contact. There is no evidence that HIV is spread by mosquitoes, lice, bed bugs, in swimming pools, or by sharing cups, eating and cooking utensils, toilets and air space with an infected individual. In other words, HIV infection and AIDS are not contagious.

1.1.4 Mechanism of action of the HIV virus

Although it is clear that HIV is the underlying cause of AIDS and AIDS-related disease, it's origin, as already discussed, remains obscure. Serological evidence suggests that HIV infection in central Africa pre-dates infection in North America. Analysis of the HIV-1 genetic material, or genome, has suggested an origin in chimpanzees while, in the case of HIV-2, genome similarity points to an origin in a

species of monkey. In both cases the consumption of these 'bush meats' has been incriminated in the transmission to the human host. HIV appears to have mutated and shifted its host range and virulence, explaining how a new pathogenic retrovirus could arise in humans. Its virulence may since have been amplified as a result of travel, population dislocation and promiscuous sexual contact, with a resultant rapid passage of the virus.

HIV is specifically known as a *retrovirus*. Retroviruses are so named because their genomes encode an enzyme called *reverse transcriptase*, which allows DNA (the virus 'blueprint') to be transcribed from RNA (a more basic form of DNA). Thus, HIV can make copies of its own genome, as DNA, in host cells such as the human CD4 'helper' white blood cells (lymphocytes). The viral DNA becomes integrated in the lymphocyte genome, and this forms the basis for chronic HIV infection. Such integration of the HIV genome into host cells is a formidable barrier to any antiviral treatment that would not only suppress but also eradicate the infection. However the basis of modern treatment is the use of *combinations* of antiretroviral agents which has altered the mechanism of action of the HIV virus and transformed the prognosis for HIV-positive individuals.

1.1.5 Early history and development of the HIV epidemic

In 1981 doctors in the USA began to notice a series of unusual infections in gay men in Los Angeles, New York, and other big cities. These infections had previously been extremely rare except amongst people whose immune systems had been seriously weakened in some way. The most life-threatening seemed to be *Pneumocystis carinii* pneumonia and Kaposi's sarcoma. However a whole range of other severe infections and tumours had also been detected amongst gay men in these cities.

In addition, doctors had begun to find persistently swollen lymph glands in otherwise perfectly healthy gay men. The majority of these men stayed healthy for months or

years after diagnosis. However some went on quickly to develop the infections mentioned above.

These problems were first reported in June 1981 by the U.S. Centre for Disease Control (CDC). A CDC report brought the syndrome to the attention of doctors in other U.S. cities. By late 1981 researchers were beginning to link these *opportunistic infections* to damage to the immune systems of those who were affected. Even though the condition became known early on as AIDS, its cause and modes of transmission were not immediately obvious. The virus now known to cause AIDS in a proportion of those infected was discovered in France in 1983 and given various names. Since 1986 it has generally been referred to as HIV.

In 1984 a test for detecting antibodies to HIV was developed and this revealed that only a relatively small proportion of people with HIV had gone on to develop AIDS. AIDS was simply one end of a spectrum of different effects of HIV infection, ranging from staying well through to life-threatening opportunistic illnesses.

In 1986 HIV-2 was discovered, and some researchers are claiming there may be other different strains of the virus. Fortunately these all appear to behave in the same way and this need not change advice about transmission, prevention, safer sex and hygiene. HIV-2 has not been studied as extensively as HIV-1. However it seems that it causes less severe immune damage than HIV-1 in the long term, and that people with HIV-2 may on average stay healthy for longer than those with HIV-1. In particular HIV-2 has been isolated in people with West African connections.

95% of all new HIV infections occur in developing countries and continents, the epidemic being concentrated in sub-Saharan Africa and south-east Asia. It is now recognised that cases of AIDS were first seen in Central Africa in the 1970s even though at that time it was not recognised as such. Prevalence is at its highest among prostitutes (50-90%) and those attending departments for sexually transmitted

diseases and antenatal clinics (60-70%). In the developing world, HIV is spread mainly by heterosexual intercourse.

In North America and the UK the first wave of the epidemic occurred in homosexual men. Even though infections amongst men who have sex with men still arise, an increasing proportion of new infections are occurring amongst intravenous drug users sharing needles and equipment. There is also an increase amongst heterosexuals in both the USA and the UK. Thus the nature of the epidemic in the UK is changing with more heterosexual transmission. In the UK 12% of adult cases of AIDS have occurred in women, 70% of which have resulted from heterosexual intercourse. In 2000 there were more new annual infections of HIV than ever before and for the first time more were occurring as a result of heterosexual sex than men having sex with men (SCIEH, 2000).

The advent of an effective antibody test in 1984 has created more clarity regarding the changing prevalence and natural history of HIV infection. It has been observed that the proportion of individuals infected needs to be high before cases of AIDS start to become apparent. It also highlights the importance of health education campaigns early in the epidemic, when the seroprevalence of HIV is low. Once cases of AIDS start to appear the epidemic drives itself and a much greater effort is required in terms of control and medical care.

Within countries a considerable variation in seroprevalence rates for HIV can become apparent. Over 70% of cases of AIDS and HIV infection within the UK occur and are observed in London and the surrounding area. Among different groups geographical differences are also noticed. For example, the rates among injecting drug users are higher in Edinburgh than in London, and for gay men higher in London than anywhere else in the UK.

1.1.5.1 Prevalence and Patterns of HIV Infection in Lothian

In 1985 a high prevalence of HIV was discovered in injecting drug users in Lothian, which led Edinburgh to be dubbed "The AIDS capital of Europe".

Figure 1 (page 21) shows the large numbers found to be infected when the test for HIV became available in 1985 and testing of stored blood showed that the majority of drug users had become positive in 1983 and 1984. In total, 1,684 people have been tested and/or treated in Lothian to June 2002. Of these, 684 are known to have died; 392 of these were drug users. After 1985 and 1986, when special clinics were set up to counsel and test intravenous drug users (IDUs) who might have been at risk, the numbers rapidly fell, probably because HIV had infected all those at risk in the IDU population. HIV had probably saturated the population of an estimated 2,000 injectors at that time. Since the early 1990s the numbers being tested positive have remained fairly static, with between 60 and 80 cases diagnosed in Lothian each year. Most of those diagnosed latterly have acquired HIV through sexual transmission, either heterosexual or homosexual.

Figure 2 (page 21) shows the incidence of both AIDS cases and deaths in all groups. In common with reports from all over the developed world, when combination therapy became readily available in 1987, the incidence of opportunistic infections, leading to an AIDS diagnosis rapidly declined as did deaths overall. Until 1987 the number of new infections were matched by the number of deaths, so that the absolute number of HIV positive people in Lothian remained relatively static. Since 1987, the number of people attending clinics for treatment, and the numbers receiving treatment, have steadily risen. Similarly, concerns have been raised about escalating cost, about the possibility of complacency over transmission, and the possibility of transmission of resistant virus.

Figure 3 (page 22) shows the frequencies of individuals by risk group, who are currently receiving treatment. In March 2002, the month for which these latest

figures are available, there were over 450 people receiving combination therapy. The majority were on 3 drug regimes, but an increasing number (170) of people were observed on regimes containing more than 3 drugs. This is one indication of the struggle that clinicians are experiencing in trying complex regimes with people who have first attended ill, and therefore need highly potent regimes, or in patients who have tried a number of regimes in the past and have developed resistance. Much of the latter can be ascribed to adherence problems, for a number of reasons, which will be explored in later sections of this introduction.

Figure 1: Frequency of HIV positive results by year for All and IDUs risk groups

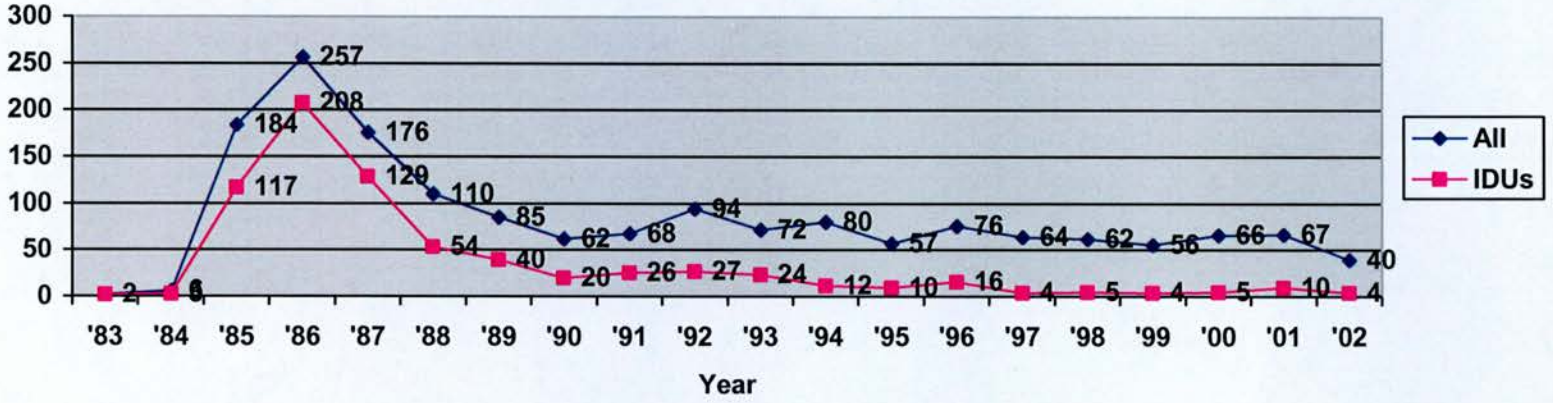


Figure 2: Incidence of AIDS and deaths across all groups in Lothian

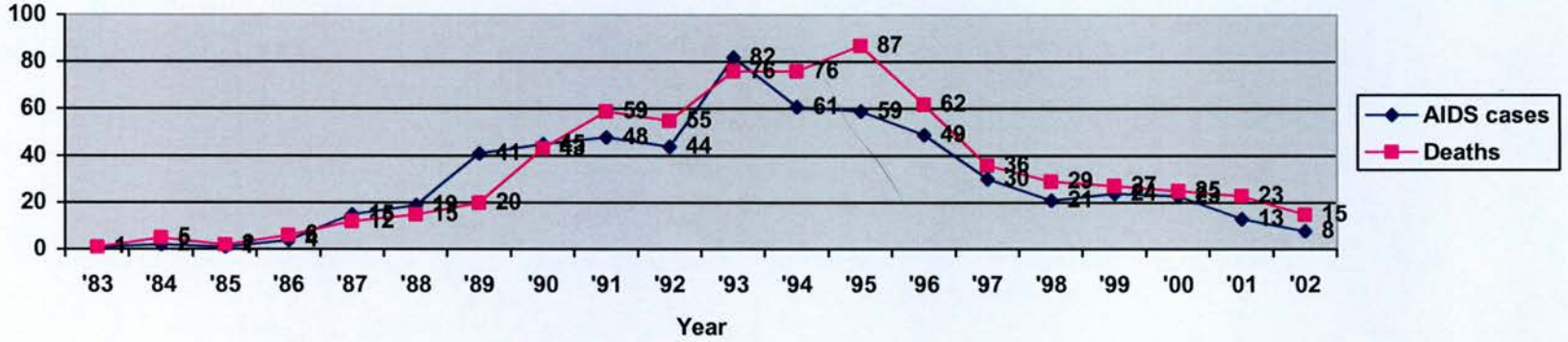
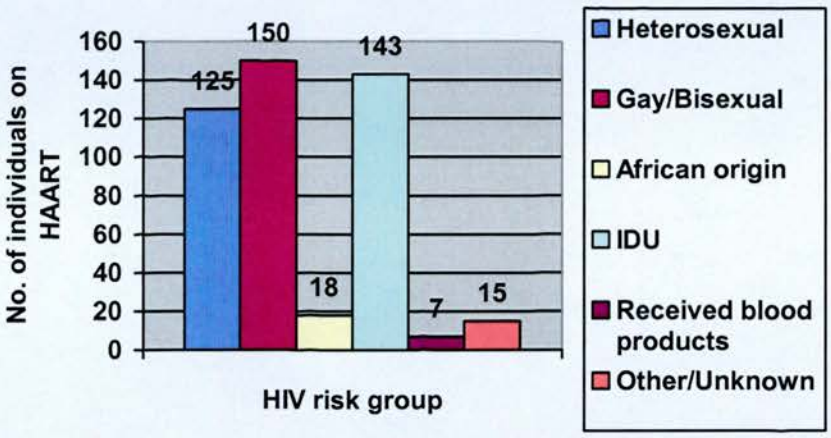


Figure 3: ***Number of individuals on antiretroviral treatment by risk category of HIV infection (Lothian)***



The use of highly active antiretroviral therapy (HAART) as a treatment strategy in resource-rich countries has resulted in an increase in life expectancy. In combination with the increase in new HIV infections, this means that the prevalent pool of those infected, and potentially infectious, is increasing. This presents a continuing challenge for health promotion and a re-statement of the importance of safe sex techniques, particularly condom use.

1.1.6 Treatment of HIV infection

The treatment of HIV infection can be largely divided into: 1) specific antiviral agents that inhibit viral replication, and 2) measures that either treat or prevent (prophylaxis) it's complications – namely opportunistic infections and tumours. Advances in the treatment of HIV infection have resulted in marked falls in the number of reported new AIDS cases and deaths in the developed world since 1996. The main reasons for this have been effective antiretroviral therapy regimens which substantially inhibit HIV replication and allow durable improvements in the immune system. In those who are severely immunosuppressed the treatment and prophylaxis

of opportunistic infections remains important. The most effective way to prevent first episodes or recurrence of opportunistic infections is treatment with antiretroviral drugs. One strategy to provide more potent suppression of HIV, and more durable suppression by delaying the emergence of resistant virus, is the use of combination therapies. Clinical trials over recent years have clearly demonstrated the superiority of combination therapies over monotherapies in achieving improved clinical outcomes.

1.1.6.1 The theory of early intervention

Until recently, the issue of when to start treatment for HIV/AIDS has been dominated by the theory of early intervention. The idea of early intervention is to provide prompt medical treatment relatively early in the course of HIV infection, before clinical illness has developed, with the aim of preventing or delaying the appearance of symptoms. It is considered a form of prophylaxis against developing symptomatic HIV disease or AIDS.

There are three possible approaches to early intervention:

- Using anti-HIV drug combinations
- Using immune stimulants or therapeutic vaccines
- Using prophylaxis against opportunistic conditions

It is also worth noting that many people regard maximising their general state of health as an excellent early intervention, although it does not strictly fit the exact definition of early intervention. This may range from giving up smoking or other drugs, taking exercise, or improving diet, to stress reduction, relaxation, and other alternative therapies. No scientific studies to date have provided strong evidence that, in themselves, these pursuits make a direct difference.

Since the mid-nineties, antiretroviral therapy has taken centre stage in HIV treatment. There was a strong push to 'hit hard, hit early' in order to prevent damage

to the immune system and the illnesses that follow. It is also felt that current drugs have a greater chance of reducing viral load to undetectable levels if the treatment starts when viral load is relatively low (below 50,000 copies).

However, over the last three years there has been a shift away from early treatment in the asymptomatic phase of HIV infection, for several reasons. There is growing concern about the long-term toxicities of HAART and long-term side effects may lower quality of life. Secondly, the clinical benefits of treatment begun before the onset of advanced disease remain largely unproven. Finally, preliminary evidence from several large studies shows no advantage to starting treatment with a CD4 count[2] above 350 compared with starting treatment with a CD4 count between 200-350, at least in the short-term (1-2 years). There is uncertainty as to how long the drugs should be taken for and resistance may develop if the treatment fails. This may leave a person cross-resistant to many of the drugs now available. During early 2001, revised British and US guidelines moved away from early treatment strategies in people with chronic infection.

Two different blood tests are used to monitor the progress of the virus, *CD4 count* and *viral load count*. Because CD4 count and viral load are directly influenced by antiretroviral drugs, both counts have also been used as a measure of an individual's adherence to their medication regimen.

1.1.6.2 CD4 Count

CD4 cells are the white blood cells (lymphocytes) in the immune system which are targeted by HIV. A CD4 count measures the number of these cells contained in a cubic millimetre of blood. The lower the CD4 count, the more damage the immune system has sustained from HIV infection. An individual with a CD4 count less than 200 cells/mm^3 would be described as severely immunosuppressed.

1.1.6.3 Viral Load

Viral load count is a measure of the amount of HIV in the blood (the number of copies of HIV in 1 millilitre of blood plasma). Reducing viral load has been shown to reduce the risk of dying from AIDS. It has also been shown to improve the health of people with AIDS-related illnesses. Reducing viral load and keeping it down is the aim of antiretroviral therapy. The aim of treatment should be to achieve and maintain undetectable viral load (below 50 copies/ml of blood plasma). For people who have taken several anti-HIV regimens, the aim of treatment may be to boost CD4 cell count rather than to achieve undetectable viral load. To strive for undetectable viral load may mean using many drugs which may in turn produce severe side-effects.

1.1.6.4 Antiretroviral therapy for HIV/AIDS

HIV contains nine genes, which carry all the information needed to make new viruses. When HIV locks onto a CD4 lymphocyte its genetic material is absorbed into the cell. HIV then makes a copy of its genetic information. This is called a provirus. HIV uses an enzyme of its own, called reverse transcriptase, to do this. Drugs called reverse transcriptase inhibitors can stop the virus from making these copies. The provirus, or copy, is then inserted into the genetic code of the host cell. HIV uses another of its enzymes, called integrase, to do this. The provirus is put into the genetic code, or genome, by cutting the genome and slipping in the HIV provirus. Drugs are being developed to stop integrase from doing this.

Some of HIV's genes can instruct the cell to use its own machinery to make new viruses. When the cell receives these instructions, it makes another copy of the provirus that is bound up in its genetic material. This copy is then used to generate the production of new viruses from materials supplied by the cell. In effect, the cell

[2] CD4 Count – The number of CD4 cells in a microlitre of blood plasma. HIV attacks CD4 cells and their number falls as the infection gets more serious.

has been hijacked by HIV and turned into a virus factory. Each cell can produce dozens, if not hundreds, of virions (virus copies).

The new viral building blocks need to be assimilated. Another HIV enzyme, called protease, is produced to do this job. Drugs called protease inhibitors can stop this process. If viruses can be assembled they are packaged in the cell wall of the host cell. They are pushed through the cell wall and are then free to enter the bloodstream and pass into other cells.

Thus antiretroviral drugs target specific stages of the HIV life cycle, preventing it from reproducing itself. There are currently three classes of antiretroviral agents, each attempting to disable the virus at a different stage of it's life cycle: the *nucleoside* and *non-nucleoside reverse transcriptase inhibitors* and the *protease inhibitors*.

1.1.6.4.1 Reverse transcriptase inhibitors

Reverse transcriptase is a unique characteristic of retroviruses such as HIV. Once HIV releases its genetic material into a human host cell, the reverse transcriptase enzyme helps assimilate the protein building blocks in the cell to make more copies of viral DNA. Reverse transcriptase inhibitors block this process.

The main class of reverse transcriptase inhibitors comprises the nucleoside analogue drugs. Nucleoside reverse transcriptase inhibitors include: *AZT*, *ddI*, *ddC*, *abacavir*, *3TC* and *d4T*. Non-nucleoside reverse transcriptase inhibitors include: *nevirapine*, *delavirdine*, and *efavirenz*.

1.1.6.4.2 Protease inhibitors

Protease inhibitors also act against the enzyme that HIV uses to break up large proteins into the smaller proteins from which the new viral particles are produced. New HIV particles produced in the presence of protease inhibitors are immature and

non-infectious. The protease inhibitor drugs include: *indinavir*, *saquinavir*, *ritonavir*, *nelfinavir*, and *amprenavir*.

1.1.6.5 Combination therapy

HIV makes numerous mistakes when it copies itself. Unlike human cells it is unable to detect these errors or remove them. Many of these copies are so faulty that they cannot infect other cells, or they will only reproduce very slowly. These copies of the HIV virus are those that are targeted by antiretroviral drugs. However, some viral copies will develop genetic changes which allow them to make copies even when antiretroviral drugs are around. This is known as *drug resistance*.

Every antiretroviral drug works against a slightly different part of HIV's protease or reverse transcriptase enzymes. Each enzyme is made up of many pairs of chemicals called amino acids. Sometimes these amino acids will be placed in different positions as a result of faulty copying. This gives the virus the ability to continue making copies even when high levels of an antiretroviral drug are present. However another antiretroviral drug may have more success in stopping reverse transcriptase from working because it's target is a different set of amino acids on the 'mutant' virus. It is for this reason that a combination of drugs in therapy is more effective than using one drug in isolation to fight the virus.

Combination therapy can use different drugs, which attack the same enzyme, or it can use a combination of drugs, which attack several different enzymes simultaneously. It is not known which approach is best in the long-term. Combinations of two or more drugs have been shown to substantially reduce the risk of disease progression and death. The best results are usually seen with combinations that include a protease inhibitor and reverse transcriptase inhibitors. Currently, combinations of at least three anti-HIV drugs (triple therapy) are the standard of treatment. Individuals considering treatment need to discuss the most suitable drug combination with their doctor. A number of factors need to be examined including

current state of health, potential side effects, and how taking the drugs will fit into their lifestyle. The best combination for anyone is that which best fits their lifestyle *and* achieves maximum suppression of HIV.

1.1.6.6 Side effects of antiretroviral therapy

The drugs used in combination therapy are particularly powerful drugs, many of which have strong side-effects. Additionally, the more drugs an individual takes in combination, the greater the chance of unwanted interactions between them. The side-effects of most drugs are well established. Information on toxicities is gathered during clinical trials and reports from prescribing doctors. However, many drugs used by people with HIV are relatively new and the urgent need for effective medications has meant that many anti-HIV drugs are released onto the market after only a relatively small number of people have taken them for a relatively short period of time. Information on side-effects and adverse drug interactions can be less complete than with other medications.

In the age of HAART, drug side-effects are a common cause of ill-health among people with undetectable viral load or asymptomatic HIV disease. Allergic side-effects occur when the immune system reacts to a drug by causing symptoms such as a rash or a fever. Allergic reactions will occur despite the dose of drug taken. Starting at a low dose can desensitise the immune system to the allergic reaction. Allergic reactions can be so serious that they become life-threatening. Other side-effects may be caused directly by unwanted effects of the drug itself, rather than by the immune system's response. A wide range of potential side-effects is possible and may include: anaemia, nausea, diarrhoea, bloating, abdominal discomfort, headache, dizziness, general malaise, fatigue, and reduced sex drive.

Side-effects such as nausea, vomiting, diarrhoea, abdominal pain, and headache and dizziness, tend to be associated with the time at which drug levels reach their peak in the blood. Given the frequency of daily doses, this is why side-effects may occur

regularly at certain times of the day. The inconvenience of these side-effects may be reduced by adjusting the time at which particular medications are taken throughout the day. However this will depend on individual eating schedules and the need to take medications with food or on an empty stomach. Frequently, even more drugs need to be taken to deal with unwanted side-effects, such as anti-nausea or anti-diarrhoea medicines. This can exacerbate the frequency of pill-taking episodes and make medication adherence even more problematic.

Other side-effects, associated with the long-term use of antiretrovirals, include lipodystrophy, wasting of the arms, legs and face, and metabolic abnormalities including high blood lipids, insulin resistance and high lactate levels. Coping with side-effects can become a constant challenge for individuals taking antiretroviral therapy. Consequently, they can make it very difficult for people to successfully adhere to therapeutic levels of antiretroviral regimens.

1.1.6.7 Resistance to antiretroviral drugs

Resistance can develop against all current antiretroviral drugs and is a major factor contributing to therapy failure. Resistance occurs when HIV mutants emerge which can reproduce in the presence of a drug. The mutated virus forms the basis of a new virus population because they can reproduce despite the antiretroviral drug being present. Once resistance to one drug has emerged, this virus population may also be resistant to other drugs not yet taken. This is called cross-resistance. Drug resistant viruses can be transmitted and 10-15% of patients presenting with primary HIV infection already have mutations associated with drug resistance (Gottlieb, 2000). Opportunity for resistance is greatly reduced if *every* prescribed dose of antiretroviral drug is taken. A missed dose causes blood concentrations of the drug to fall, making it easier for mutant viruses to reproduce. Patients who achieve sustained falls in plasma viral load to <400 copies/ml are less likely to develop mutations associated with drug resistance than those who do not. The more often doses are missed, the more likely it is that resistant viruses will emerge. Resistance

testing is possible, and can guide a choice of therapy in individuals changing treatment and in those recently infected.

Poor adherence to combination therapy is a *major* contributor to developing resistance to antiretroviral drugs.

1.1.6.8 AIDS, survival and mortality in the HAART era

Since mid-1996 the widespread use of HAART has seen a dramatic decline in the number of AIDS-related deaths in many countries. A concommitant increase in the number of people living with HIV and AIDS has also been observed. Research presented at the 39th Interscience Conference on Antimicrobial Agents and Chemotherapy suggests that the incidence of AIDS-defining events has fallen dramatically across Europe during the HAART era. Data from 7,200 participants of an HIV positive cohort found that 31% became ill within a year in 1994, but that this rate had fallen to 3% by 1998 (Reiter et al, 1999). This period was marked by the gradual introduction of anti-HIV therapies. Death rates also fell between September 1994 to March 1998 from 23.3 deaths to 4.1 deaths per 100 persons. The decline in mortality was most striking among people with very low CD4 counts. Among people with CD4 counts between 50-99, the death rate fell from 20% to 7% during the study period. Among people with CD4 counts below 50, the death rate fell from 60% to 8%. Increased survival was strongly associated with combination therapy. For people not on treatment the death rate was 65.4%. For those on dual and triple combinations of treatment, the death rates were 7.5% and 3.4% respectively. The lowest death rate was observed among those who commenced treatment with a triple combination (Mocroft et al, 1998). A study of 421 people with HIV attending the Royal Free Hospital in London who commenced HAART, found that incidence of death among patients on treatment was 1/6th of pre-HAART levels, while the incidence of new AIDS-defining illnesses and hospital admissions was 1/7th and 1/5th respectively (Mocroft et al, 2000).

American research also reveals the dramatic impact of antiretroviral therapy on the health and survival of people with HIV. The number of AIDS-related deaths in New York City for example, fell by 63% between 1995 and 1997. The actual number of deaths has fallen from over 7,000 to 2,625 per year. However, this decline in the number of AIDS deaths has slowed. In the USA there were 17,047 deaths from AIDS in 1998 compared with 21,222 in 1997. The slowing of the decline in deaths suggests a failure of current treatments (due to drug resistance, toxicities and other causes).

1.2 Adherence

1.2.1 Introduction to treatment adherence

Getting people to take their medication as prescribed has always been a problem for medicine and a concept long known to health psychology (Buckalew & Sallis, 1986; Ley, 1997). Whether or not medications are taken, forgotten or discarded very often depends upon the differences and diversities of the individual lives of patients. Thus medication adherence is widely perceived to be beyond the influence of clinicians. This section considers the issue of non-adherence among individuals with chronic or life-threatening conditions including HIV/AIDS.

1.2.2 Adherence and chronic illness - the research base

The magnitude of the problem of poor adherence to long-term medical regimens for chronic disease has been well documented over the last 30 years or more. The rates have changed little over that time period (Dunbar-Jacob, Dwyer & Dunning, 1991). Various research studies have suggested that as much as 80% of patients would not follow their treatment programme sufficiently in order to achieve therapeutic benefit (Dunbar-Jacob, Burke and Puczynski, 1995). Furthermore, the problem of non-adherence crosses age groups, diagnoses, and socioeconomic variables as well as various treatment regimens (Goodall & Halford, 1991). Meichenbaum and Turk (1987) estimated slightly improved estimates of medication non-adherence, across various illnesses, typically ranging from 30% to 60%. However, the non-adherence percentage rate was observed to be greatest when the patients studied were reported as symptom-free. This is of particular relevance when applied to HIV/AIDS where individuals can be asymptomatic for considerably lengthy periods of time.

Medication remains the most widely studied regimen with the vast majority of studies occurring in chronic disease. One of the most commonly studied is hypertension. Average rates of adherence among people with hypertension tend to

average about 64% (Dunbar-Jacob, Dwyer and Dunning, 1991) and even with great attention to improving these rates over the past two decades, significantly little change has occurred. Highest rates have tended to be observed in family practice sites with hospital out-patient clinics showing the smallest proportion of adherent patients (Dunbar, Dunning, Dwyer, Burke & Snetselaar, 1991). Adherence rates among people with other chronic disorders are similarly problematic. 40% to 60% of people with rheumatoid arthritis adhere to medication targeting inflammation of the joints (Hicks, 1985), among people with chronic pulmonary disease more than 50% report missing or discontinuing medication (Dolce et al, 1991), and in patients receiving organ transplants adherence rates of 57% to 85% have been reported (Rovelli et al, 1989; Schweitzer et al, 1990).

Although adherence to medication regimens has been most widely studied, there is also evidence that making changes in other health-related behaviours, such as diet and exercise, is even more difficult (Lynch D.J. et al, 2000; Lynch D.J. et al, 1992).

The rates reported for other specific diseases are similar to those stated above. Despite as few as 20% and as many as 80% of people adhering to a specific treatment medical regimen within a specific sample, overall adherence studies appear to suggest that a crude estimate of between ½ to ¾ of patients across a broad range of diseases adhere to treatment, at least sufficiently enough to obtain therapeutic benefit. These rates of adherence are problematic whether the disease is symptomatic or not (e.g., rheumatoid arthritis vs. hypertension or asymptomatic HIV infection) and whether the disorder is or is not more immediately life-threatening (e.g., organ transplantation vs. hypercholesterolemia[3]). The research into adherence and chronic illness will be returned to in Section 3 of this chapter, which also considers the extent of the role of personality characteristics.

1.2.3 Research into adherence to HAART

The strict medication regimens of HAART make adherence a constant problem for HIV infected individuals[4]. Currently, HIV clinics, care services and HIV prevention organisations are all developing initiatives focussed on confronting the problem of adherence to HAART. The issue of who is best placed to address this problem remains largely open. There is therefore an opportunity for clinical psychology to apply research skills to this area and potentially offer suggestions for intervention. Any enthusiasm to respond to the problem is fully justified given the crucial role of adherence in the long-term success of antiretroviral therapy. Ultimately, the challenge adhering to HAART has to be met by the patients themselves, as it is they who are left with the task of taking medications on a daily and routine basis. This would imply that only self-help in its most basic form would ensure that the process takes place as it should.

Recent evidence has suggested that most people with HIV cope relatively well with the demands of adherence to HAART (AIDS Treatment Update, Adherence special issue, 1999). In a qualitative study of HAART (Anderson & Weatherburn, 1998), participants described their experiences of learning to live with the pills. Individual stories were characterised by the process of adjusting to the routines of their daily lives; integrating the treatment schedule meant making the pills as routine as everything else. Most participants described daily routines with varying degrees of acceptance, frustration and resentment. However all shared a common commitment

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[3] Hypercholesterolemia – A genetic disease in which too much cholesterol is present in the blood. There is no cure but it can be controlled by diet regimens.

[4] The experience of an individual, from the thesis research sample, reflects the strict requirements of a HAART regimen: Mr 'A' is 52 years old and, although currently unemployed, is a part-time voluntary worker. He is on a current combination therapy of four different antiretroviral drugs; *Abacavir (12 per day), saquinavir (3 per day), Ritonavir (3 per day) & Efavirenz (3 per day).* Mr A takes a total of 21 antiretroviral pills every day. He has specific instructions to take these pills twice per day, at 10am & 10pm. In addition some of these pills are to be taken with food and some not. If Mr A deviates from any of these instructions the drugs may not have any therapeutic benefit. Mr A finds some of the pills almost too large to swallow even with a drink. He reports that he misses a dose about once or twice every week. He sometimes takes his pills at a different time than that specified – around four times every month. He cites routine interruptions and forgetfulness as common reasons for not adhering accurately to his regimen. He has no currently reported adverse drug side-effects, but the daily inconvenience of taking his medication, especially during work, has resulted in him considering a 'drug holiday'. In addition to his antiretrovirals, Mr A takes a further 7 prescription pills every day for anxiety, anti-sickness, and to boost thiamine and folic acid levels. In total Mr A takes *28* pills *every* day for the foreseeable future.

to taking the pills and to making whatever adjustments to life that were necessary. Furthermore, in a recent national study (Anderson & Weatherburn, 1999), almost all (97%) of those who were taking HAART agreed with the statement that 'HIV is still a very serious condition'. 94% said that 'HIV can become resistant to treatments, especially if they are not taken properly'. Therefore, not only is HIV still perceived to be a serious medical condition, but the consequences of non-adherence are also understood to be very serious.

The incentives for adhering to HAART are unusual among treatments for chronic diseases. The general research literature on adherence to medications proposes that a willingness to take treatment depends on assessment of the severity of the illness and susceptibility to it. In other words, if you do not think that your illness is very serious, or think that it will not affect you much, you are unlikely to take medications properly. The vast majority of people with HIV are in no doubt where they stand with these issues. Consequently, although rates of adherence average around 50% in many other conditions (Blackwell, 1996), people with HIV miss a dose much more rarely. The contrast with research into other illnesses draws attention to how comparatively well people with HIV are doing in adhering to their medications. Nevertheless, due to the life-threatening mechanism of HIV infection, a particularly high level of adherence is essential if viral suppression is to be sustained. HIV disease is associated with all the predictors of low adherence: long duration of treatment, preventative rather than curative treatment, asymptomatic periods, and frequent and complex medication dosing. Non-adherence is related to viral resistance (Condra et al, 1995), a problem that affects not only the individual under treatment but also public health concerns about future treatment and containment of HIV infection. This then makes non-adherence a major problem among patients treated for HIV infection. Before the HIV era, adherence levels above 80% were seen as satisfactory, but now the target is 100%. A number of recent studies have reported on the levels of adherence to HIV therapies (Belzer, Fuchs, Luffman and Tucker, 1999; Gordillo et al, 1998; Kastrissios, Suarez and Katzenstein, 1998). They

have adopted various means of measuring adherence including self-report, pill count, pharmacy refill records and plasma drug concentrations. The data from these studies suggests that a consistent minority of individuals do not adhere at maximum levels. These studies are mostly cross-sectional in design meaning a shortage of evidence of adherence over time. It is therefore unclear whether some patients never adhere or whether all patients sometimes do not adhere. On average, rates of adherence to antiretroviral therapy range from 50% to 70%. Table 1 (page 39) presents a list of recent studies that have documented rates of adherence to HIV antiretroviral treatment.

Table 1: Summary of recent studies of adherence to HIV antiretroviral therapy

Study	n	Adherence measured by:	Outcome
Muma et al. (1995)	52	Self report	42.5% compliant with Zidovudine
Singh et al. (1996)	46	Computerised pharmacy refill records	63% compliant (patients filling >80% of their prescriptions
Kastrissios et al. (1998)	41	Daily pill intake of 4 antiretrovirals (Zidovudine, ddC, ddI, matched placebo)	Prescribed Zidovudine, ddC, ddI taken by 88%, 84%, 82% respectively. But only 55%, 66%, 79% at prescribed frequency.
Kastrissios et al. (1998)	722	Plasma drug concentrations	75% had detectable prescribed drug
Eldred et al. (1999)	244	Self report / Medical record/ Urine assay	60% reported ≥80% antiretroviral adherence in previous 7 days
Mostashari et al. (1998)	102 (female prisoners)	Self report and pill count	62% adherent
Gordillo et al. (1999)	366	Self report and pill count	Good adherence by 58%
Belzer et al. (1999)	31 (young people)	Self report	65% reported >90% compliance in previous 90 days

Zidovudine, ddC, and ddI are types of antiretroviral drugs

1.2.4 Reasons for non-adherence in HIV and other life-threatening illnesses

In general, beyond life-threatening or chronic illnesses, as the population continues to age and cost-containment pressures increase, healthcare professionals will constantly be challenged to find ways to empower patients to play a greater role in the management of their illnesses. Obviously, one avenue towards achieving this is by patients being trusted to adhere to their medication regimens. Medication regimens are dispensed with the fundamental expectation that they will be taken exactly as prescribed. Non-adherence has negative consequences for the patient, the clinician, the provider, and even the medical researchers who work to establish the value of the medication for the target population. The current composite issues surrounding the particularly high rates of non-adherence in chronic illnesses, especially HIV/AIDS, are well illustrated in an early paper by Sackett and Snow (1979). They reported that 77% of patients demonstrated degrees of compliance with their medication regimen when the treatment was designed to *cure* a disease, and only 63% of patients complied when treatment was aimed at *prevention*. Furthermore, when medication was to be taken over a long period, as is the case with HIV/AIDS, compliance rates dropped dramatically to around 50% for either prevention or cure.

As can already be assumed, many factors are involved in patient non-adherence: disease characteristics, medication side-effects, duration of treatment, frequency of dosing, complexity of treatment, severity of the disease, socioeconomic factors and psychosocial variables. Adherence is less likely over long treatment periods, and even when daily doses require relatively minor increases from one pill to four pills (Kramer, 1995). Schedules calling for medication to be taken four or more times a day appear to create an unnatural division of the day for most people, increasing the potential for non-adherence. The majority of patients may also be trying to please their physicians, typically giving the often convincing impression that they have been following, or intend to follow, the physician's medication directives. Unsurprisingly, overly anxious patients forget more of what they are told by their

physician. Studies have reported that 40% to 60% of patients could not correctly report what their physician expected of them 10 to 80 minutes after their consultation (Ley & Spellman, 1976). If the information presented is consistent with previously held beliefs about the disease and about what medication can and cannot do, patients are more likely to adhere to the medication regimen (DiMatteo and DiNicola, 1982).

People with HIV do not usually miss doses because of a lack of motivation to take treatments or because they choose to give greater priority to other aspects of their lives. 'Drug holidays' for special reasons are often taken, but deliberate non-adherence is rare. A study in San Francisco (Chesney, 1997) reported that the most common reasons for missed doses were forgetfulness (40%), sleeping through time of dose (37%), absence from home (34%), routine interruptions (27%) and distractions (22%). Another very important reason for lack of adherence is a poor tolerability of the drugs.

In summary, forgetfulness and failure to plan ahead would appear to be the main reasons for non-adherence. Forgetting happens for many reasons - being too busy, being distracted by work or pleasure. Sleeping through a dose is evidence of failure to plan ahead. Change, interruption or intrusion into a routine undermines expectations and diverts reminders to take medications. As individuals' lives are so unpredictable and variable, it becomes almost impossible to predict who will or will not be adherent.

1.2.5 Developing a psychological approach to non-adherence to HAART

By increasing an understanding of adherence factors in HIV, research can become more systematic and interventions may then be generated and subsequently evaluated. Dunbar-Jacob et al (1995), and more recently Sherr (2000), suggest that medical adherence, in general, can be studied from four main perspectives: (1) the

patient or person, (2) the preparation or medication, (3) the healthcare provider and (4) the setting or environment.

1.2.5.1 Patient characteristics

The least relevant factors appear to be demographic strata. Age (with the exception of adolescence), gender, marital status (with the exception of dietary adherence), and socioeconomic status have not been consistently related to adherence. The impact of culture or ethnicity on adherence is under researched. However, some studies that examined these issues have reported significant differences in adherence patterns across cultures (Dolce et al, 1991). One study has found that a specific cultural cohort of patients (Hispanic) were more likely to comply with medication recommendations when their clinicians demonstrated some understanding of their cultural norms and practices (Ruiz and Ruiz, 1983). There has been a recent increase in the number of studies addressing the impact of specific cognitive coping strategies, such as denial, learned resourcefulness, and helplessness, on patient adherence specific to HIV. These studies have produced significant associations and will be discussed later. Selective cognitive elements have been associated with adherence in other illnesses. Sherbourne et al (1992) noted that avoidant coping was associated with adherence. Research within the Common Sense Model of Illness, has noted that cognitive constructions of the illness, or the model the patient holds of their disease and its course, are also associated with adherence (Baumann et al, 1989). Self-efficacy has also been associated with adherence in cancer treatment (Lev, 1997). Personality characteristics have been the least studied factors in research into medication adherence. A wider discussion of the research into personality and adherence will be returned to further into this report. A summary of the most relevant patient characteristics, predictive or non-predictive of adherence can be referred to in Table 2 (page 43).

Table 2. Summary of studies of predictors of adherence to HIV antiretroviral therapy

Study	n	Predictors of adherence	Not associated with adherence	Predictors of non-adherence
Muma et al. (1995)	52			Scepticism of efficacy, ethnicity
Singh et al. (1996)	46	No IDU history, adaptive coping, lower depression scores, previous opportunistic infection, less psychological disturbance	Age, education, employment, religious support, quality of life	Ethnicity
Besch et al. (1997)	179		Age, sex, race, IDU, stage of disease	Forgetting appointments, conflicts with routine, not filling prescriptions, too many pills, feeling weak, no. of blood tests, confidentiality issues
Kastrissios et al. (1998)	41	Monotherapy rather than combination, older patients	Patient characteristics	
Eldred et al. (1998)	244	2 doses per day, dose to be taken away from home, belief in ability to adhere, presence of family	Socio-demographic characteristics, belief in efficacy of medications	
Mostashari et al. (1998)	102 (female prisoners)	Trust in medications, trust in healthcare system, interpersonal relationships with clinicians and peers	Prison	
Gordillo et al. (1998)	366	Age (32-35 years), transmission category, CD4 count, depression, perceived social support	IDU, younger age	Depression, lack of social support
Singh et al. (1999)	123	Satisfaction with social support, coping style (problem-focused & active-behavioural), Caucasian	Age, education, employment, income, history of IDU, medical regimen	Loss of motivation, hopelessness, avoidant coping, no. of medications

IDU = Intravenous Drug Use

1.2.5.2 Medication regimen characteristics

Across all medical disorders, regimen features are particularly important influences on adherence. Several dimensions of the regimen appear to be most critical. The more frequently the regimen needs to be repeated throughout the day, the greater the probability of non-adherent episodes. Also, the greater the number of separate regimens (e.g., diet plus drug as opposed to drug alone) the more likely adherence will be affected. Regimens requiring lifestyle behaviour changes complicate adherence further. With particular reference to HIV/AIDS, another critically important factor is the duration of the regimen. Adherence declines over time (Sherr, 2000). Patients on long-term treatment regimens are more likely to default with regard to their dosing circumstances.

1.2.5.3 Healthcare provider characteristics

Providers and their practices influence patient adherence. Their skills in communicating, and explaining dosing and regimens clearly, checking that instructions are understood, reviewing questions, queries and problems on a regular basis, are all key factors. Simplified instructions, specific statements and support for the process are vital.

1.2.5.4 Setting or environment characteristics

The effects of challenging social circumstances have been examined, such as those of prison settings (Mostashari et al., 1998), individuals with low levels of literacy (Kalichman S.C. et al., 1999) and that of the homeless and drug users (Sorensen, Mascovich, Wall and DePhilipps, 2000). Preconceived views of these groups need to be addressed, and the impact of particular settings on the individual's ability to carry through a therapeutic level of regimen adherence. There is evidence that these adverse social situations are not necessarily predictors of non-adherence. Furthermore, the practical and procedural aspects of the clinical practice, such as the location of clinics and the minimisation of waiting times, may play an important role in whether or not patients return for consultations and follow advice on treatment.

1.2.6 Psychological models of adherence

The above perspectives on issues of adherence can be allowed to invoke and inform a number of theories in order to help understand adherence from a psychological perspective.

1.2.6.1 Cognitive models

Cognitive models suggest that adherence is associated with cognitive variables. These variables would include memory, forgetting, recall, decision-making and comprehension of the regimens involved. Interventions aimed at addressing these cognitive aspects would be assumed to improve adherence to antiretroviral therapy. There is evidence to suggest that cognitively based interventions can significantly improve adherence. Person-centred interventions would include cognitive cues to avoid forgetting, memory aids, cognitive re-framing of decision-making processes and increasing a patient's understanding of the medication regimen. Johnson (2000), in a study of 96 HIV outpatients, reported that one coping strategy (cognitive reappraisal) and one appraisal style (helplessness/hopelessness) were significant, independent predictors of both treatment adherence and psychological well-being. It was also concluded that the prediction of treatment adherence and psychological well-being was significantly improved by using these two predictors together.

Interventions aimed at the preparation would consist of audio or visual cues to remind the person to medicate, and the simplification of dosing practicalities such as packaging to improve access to medication.

From the perspective of the provider, cognitive strategies would incorporate an improved education of dosing and regimens, reducing anxiety provoking settings and reinforcing that simplified instructions have been thoroughly understood. Variations in provider behaviour as a result of particular cognitions and beliefs have been found to be associated with adherence outcome. For example, the likelihood of a physician prescribing antiretroviral treatment has been associated with the strength

of the physician's belief in the patient's ability to adhere (Roberts & Volberding, 1998). Just as in patients, it is also feasible that lack of knowledge, forgetfulness and unfamiliarity with treatments may also affect clinicians. Provider oriented interventions such as clear record-keeping, computerised information and clear policy directives have been shown to be effective.

1.2.6.2 Social concepts

Employment, social support (or isolation), familial factors, age, financial and availability factors have also been used to help explain a lack of adherence. There may be an interaction between employment and cognitive factors in that busy employees are more likely to forget medication and thus affect adherence. There is also anecdotal evidence that in resource-poor settings, with costly and less accessible treatments, adherence is less of a problem than when medication is widely available. A wide range of challenging social circumstances have been examined and reported in the literature on adherence to antiretroviral therapy. The interaction between psychosocial factors and adherence is documented in the literature considerably more than an exploration of the cognitive factors involved.

A revealing study by deBoer (1999) examined the psychosocial responses of 70 HIV-positive gay men taking a powerful new antiretroviral treatment. Aside from 'forgetting', participant narratives revealed four commonly reported reasons for adherence lapses: chemical dependence relapse, needing to rebel, maintaining needed benefits (secondary gain) from illness status, and testing the treatment. Pre-treatment and pre-infection level of functioning also appeared important, as those who had mastered previous developmental tasks appeared more able to devote resources toward battling the disease and planning for the future. Salient issues associated with better adherence to treatment included resolution of family of origin issues and consolidation of personal, sexual, and vocational identity. Failure to have achieved a positive sexual identity, a meaningful vocational life and important interpersonal bonds prior to treatment or infection, heightened the vulnerability to re-

experience traumatic themes, which in turn manifested as a lower level of adherence to drug treatment. Results also indicated an association between higher income and higher adherence. Interestingly, the study also revealed that 'forgetting' was at times associated with wishful thinking. This highlights the combined interaction between cognitive and psychosocial factors in medication adherence.

In a study of illness behaviour, psychosocial and clinical variables among asymptomatic HIV infected individuals, significantly higher levels of medication adherence were observed in participants in a non-intravenous drug use category and who also had better social support. This study also reported significantly elevated CD4 cells among the high adhering group. Psychosocial variables resulted in influencing the tendency to interpret illness in a maladaptive way in HIV-infected subjects. Psychological stress and low CD4 cell count were the main predictors of the affective dimension of illness behaviour measured in this study (Grassi et al, 1999).

1.2.6.3 Psychodynamic models

A psychodynamic perspective would suggest that factors below the consciousness of the individual, where access is limited, mitigate against adherence. Such factors would include unconscious fears and anxieties. There is currently little empirical evidence to support this model, although interventions based upon limited qualitative data, would focus on the belief systems of the individual and an in-depth understanding of the circumstances surrounding their illness. From the provider perspective, doubts and hesitations about the medication and its efficacy would most probably be examined.

1.2.7 Measuring adherence

Adherence is essentially a *process variable* that should be evaluated in all therapeutic outcome studies and in any clinically prescribed treatment that requires a self-management component. This can be very difficult to achieve. Relief from

symptoms or the achievement of therapeutic goals may suggest that the patient is correctly following the treatment plan. However, it is no confirmation that this is indeed the case and therapeutic outcome is not necessarily a good measure of adherence.

Numerous methods of assessing adherence in chronic illness have been reported in the literature, although none are sufficiently accurate for a true standard to be identified and universally applied across treatments. As Table 3 (page 49) shows, a number of methods have been reported in the HIV research base for the measurement of adherence. An overview follows of some specific assessment methods used in chronic illnesses in general.

1.2.7.1 Self-report measures

Self-report appears to be the most commonly used method with evidence that this approach is reasonably reliable (Caron, 1985). Self-report measures are relatively easily administered and inexpensive to apply. Common approaches to self-report include patient interviews, structured questionnaires, and daily diaries. The majority of research studies examining medication adherence report the use of interview methods. Brief interviews that assess global estimates of adherence have been published (Morisky, Green and Levine, 1986; Shea, Misra, Ehrlich, Field and Francis, 1992). Limited psychometric data are available on these instruments, and they have rarely been compared with more accurate daily estimates of adherence.

Table 3: Measures of adherence in recent studies

Study	N	Adherence measure
Singh *et al.* (1996)	46	Computerised pharmacy refill records
Watson & Farley (1999)	72 (children)	Self-report, medical report, urine assays
Eldred *et al.* (1998)	Unknown	Pharmacy records: logging prescription refill
Kastrissios *et al.* (1998)	41	†Electronic devices
Kastrissios *et al.* (1998)	722 (plasma samples)	Presence of drug in plasma concentrate
Haubrich *et al.* (1999)	173	Correlated self-report with virological suppression (viral load)
Gordillo *et al.* (1998)	366	Patient self-report & pill counts
Kalichman *et al.* (1999)	182	2-day recall of treatment adherence
Hecht *et al.* (1998)	135	Self-report questionnaire: 3-day missed doses
Besch *et al.* (1997)	179	Patient & doctor report

† Electronic devices can be used as monitors in the longitudinal assessment of proxies for medication adherence

Concerns have also been raised that the nature of the questions used in the self-report interview may affect reported adherence (Burke et al, 1992; Dunbar et al, 1991). Questionnaires are also commonly used self-report measures of adherence in HIV, often integrating an assessment of other socio-demographic and psychological variables, such as social support health beliefs and questions addressing the patient-doctor relationship (see Gordillo et al, 1998, for a comprehensive methodology of adherence assessment). The literature on dietary and exercise adherence also frequently documents the use of such an approach (for example, Block et al, 1986; Schechtan, Barzilai, Rost and Fisher, 1991). Daily records or diaries are not well

documented in the research as measures of adherence in HIV. Commonly used among individuals with diabetes and dietary treatment regimens, they have the advantage of circumventing any reliance on recall required by the use of interviews and questionnaires. They also have the potential to modify the patient's behaviour as a function of self-monitoring. However, they do require that the patient be trained in effectively keeping accurate daily records. Despite this, monitoring adherence by diary appears to require further examination in relation to antiretroviral regimens before any informed judgement can be made as to its reliability as an adherence measure.

1.2.7.2 Physiological measures

A variety of physiological measures have been used as a gauge of adherence. For HIV medication adherence, such measures as the level of the drug or its metabolites in the blood plasma concentrate or urine, viral load and CD4 count have all been examined. Physiological measures rarely provide an assessment of the daily variability in adherence, but tend to identify those people who have been adherent within a relatively recent time period, close to the time of assessment. In the short-term, these measures do not identify the level of adherence, but simply classify a person as having followed or not followed some of the regimen. Physiological measures also risk being affected by individual differences in drug metabolism and the effects of antiretroviral drug resistance on CD4 counts and viral loads. Nevertheless, physiological measures remain common guides as to the adherent individual. It is also not uncommon for physiological measures to be used concurrently with self-report measures in order to increase the power of the assessment.

1.2.7.3 Pill counts and pharmacy refills

Pill counts and pharmacy refills are unique to the assessment of medication adherence. They have been used in a number of studies of adherence to HIV medication. Pill counts consist of counting the number of pills remaining from a

prescription over a defined time period and comparing that with the number of pills that should have remained. This difference is subtracted from the number of pills dispensed to determine the number that were taken. From this mathematics an adherence percentage can be calculated. Pill counts have been found to overestimate adherence in some studies of chronic illness (for example in hypertension, Rudd et al, 1990). Pharmacy refills (or pharmacy records) perform like pill counts, except the time the medication is refilled is compared with the time it should have been refilled if the patient had taken all of the medication. Adherence is estimated in a similar manner to the pill count estimate. This is a potentially accessible method of adherence assessment in antiretroviral therapy, since individuals with HIV tend to receive all their medication from the same pharmacy, thus ensuring a tightly controlled dispensing situation.

Many techniques are available for the assessment of adherence although none have been shown to be perfect. Those methods providing the most complete picture of adherence tend to be expensive and more difficult to access; whereas those providing the most detail surrounding adherence events are often the most subject to error. Existing methods are, however, sufficient to provide evidence of effective intervention, and over a certain period of time can identify estimated levels of adherence among individuals.

1.3 Personality

1.3.1 The integration of personality and adherence research

This section constitutes a broad review of the literature on the interactions between personality and HIV/AIDS. Reference to personality concepts do not arise frequently in the research behind HIV/AIDS, although some studies have applied models of personality to HIV risk behaviours, appraisal and coping styles, and quality of life issues. This section examines the available literature across some of these areas and concludes with a comprehensive critical examination of the limited role of personality in HIV/AIDS adherence research.

1.3.2 The role of personality in HIV risk behaviour

Most research into personality and HIV/AIDS is reported in the literature in the context of understanding the role of personality characteristics in HIV risk behaviour. A disturbing trend in the HIV epidemic has been the persistence of high-risk behaviours among individuals who are HIV infected. Knowledge of HIV and its transmission is insufficient in deterring certain individuals from engaging in HIV risk behaviours, suggesting that certain personality characteristics may increase the likelihood of engaging in high risk behaviour. Such individuals, who report high rates of sex and/or drug risk behaviours, include HIV infected drug users (Novotna et al, 1999), patients presenting at HIV primary care clinics (Erbelding et al, 2000), and HIV infected men who have sex with other men (Kohl et al, 1999).

There has been little empirical investigation of the influence of personality characteristics on HIV risk behaviour. However, in a revealing study Hutton and Treisman (2001) examined this area based on their own clinical observations and a review of the dimensional nature of personality [5].

[5] Most personality theories depict individuals along dimensions of *extraversion-introversion* and *stability-instability* (Costa & Widiger, 1994; Eysenck, 1990).
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They observed that of the four personality temperaments, unstable extroverts are the most prone to engage in HIV risk behaviour. They estimated 60% of their patients, referred to psychiatry, presented with this type of temperament. Their actions tended to be unpredictable and inconsistent, and they displayed a large discrepancy between thought and action. Regardless of intellectual ability or understanding of HIV, unstable extroverts were most likely to engage in behaviour associated with high risk of HIV infection. Their over-arching goal is to achieve immediate pleasure or pain removal, however risky and regardless of circumstances in an effort to eliminate low mood. Unstable extroverts in their sample were less likely to plan ahead and carry condoms and more likely to have unprotected vaginal or anal sex. They were more fixed upon the reward for sex and remarkably inattentive to the risk of acquiring an STD if they did not use a condom. Similarly, unstable extroverts were more vulnerable to drug and alcohol abuse, being drawn to these substances as a quick route to pleasure. They were also more likely to become injecting drug users because the experience is more intense, and less likely to defer this intensity in the interest of safety.

The second most common personality type observed by Hutton and Treisman, which they estimated represented about 25% of their patients, is that of the stable extrovert. Stable extroverts are also present-oriented and pleasure seeking, however their emotions are less intense and not as easily provoked. This emotional flatness is thought to generate a kind of indifference to HIV risk, as opposed to a drive to seek

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Extroversion-introversion refers to the individual's basic tendency to respond to stimuli with either excitation or inhibition. *Extroverts* are: 1) present-oriented; 2) feeling-directed; and 3) reward-seeking. Extroverts are sociable, crave excitement, take risks, and act impulsively. They tend to be care-free, inconsistent and optimistic. By contrast, *introverts* are: 1) future & past-oriented; 2) cognition-directed; and 3) consequence avoidant. Logic and function predominate over feelings. They will not engage in a pleasurable activity if it might pose a threat in the future. They tend to be orderly, reliable and rather pessimistic. The second personality dimension, stability-instability, befines the degree of emotionality or lability. The emotions of stable individuals are aroused slowly and minimally, and return quickly to baseline. By contrast, unstable individuals have intense mercurial emotions and act upon them in impulsive and irrational ways.
If the two dimensions of introversion-extroversion and stability-instability are juxtaposed, four personality types emerge: stable introverts, unstable introverts, stable extroverts and unstable extroverts.

pleasure at any cost. Stable extroverts may be at risk because they are too confident to believe that they will become HIV infected.

Introverts were found to be less common among their HIV clinic patients. Preference for cognition over feeling, and an avoidance of negative consequences, is thought to render them more likely to engage in protective and preventive behaviours. Hutton and Treisman estimated 14% of their HIV infected psychiatric patients presented with a blend of introversion and instability. Unstable introverts are typified by anxiety, low mood and pessimism. They typically seek out drugs and engage in sexual behaviours not for pleasure, but for relief or distraction from pain. They have more concern about the future and adverse outcomes. Stable introverts, comprising 1% of the sample, are typified by controlled, even-tempered personalities, and were least likely to engage in risky HIV behaviour. In fact, they hypothesized that such patients were infected with HIV as a result of a blood transfusion or an occupational needle-stick injury.

A number of empirical investigations would support the clinical observations of Hutton and Treisman, with regard to the influence of extroversion and emotional instability upon HIV risk behaviour. High extroversion has been associated with sexual promiscuity, desire for sexual novelty and multiple sex partners (Eysenck, 1976; Trobst et al, 2000). Emotional instability is related to unsafe sex practices (Fontaine, 1994) and substance abuse (McCormick et al, 1998).

1.3.3 Personality and adherence to treatment in chronic or life-threatening illness

Before any analysis of a specific interaction between personality and adherence to HIV therapy per se, it is relevant to firstly consider a review of the literature on how personality and adherence may have a relationship in terms of life-threatening illness in general. Appraisal of the literature in this area reveals a comparatively large research base upon which to construct a more explicit framework for exploring the

HIV/AIDS experience of personality and adherence factors. In an effort to reflect the wide diversity of research in this particular area some of these, often novel, studies are discussed below.

Literature reviews have typically concluded that personality factors are unrelated to adherence to general treatment programs. Therefore the following studies have been selected in order to represent, as much as possible, a cross-section of the research, early and recent, into the role of personality on adherence in chronic or life-threatening illnesses.

1.3.3.1 Personality, adherence and cancer

Evidence from research examining applications of Bandura's (1986) theory of self-efficacy in oncology suggests relationships between self-efficacy and cancer prevention, and self-efficacy and adaptation to cancer (Lev, 1997). The research found that strong perceptions of self-efficacy predicted intention to stop smoking, increased participation in screening programs, and adjustment to cancer diagnosis. Lev (1997) concluded that increased self-efficacy was associated with increased adherence to treatment.

Pugliese et al (1995) examined personality, inner experience and compliance in advanced cancer patients treated with external pumps for delivery of chemotherapy drugs. This study has particular power in that demographic strata including age, sex and level of education were controlled for in terms of their influence on response to treatment. Pugliese and colleagues note that personality variables of 'coping' and 'awareness' were positively associated with treatment compliance. Remaining personality variables held constant throughout the course of chemotherapy, across both compliant and non-compliant patients. They also found that a decrease in the inner experience variables of 'acceptance' and 'expectation', with regards to treatment, was observed in patients with low compliance. This study demonstrates

evidence for a clear link between personality characteristics and adherence in long-term treatment for chronic illness.

An earlier, and intriguing, study by Lansky (1983), considered the psychological correlates of compliance in a sample of 31 children receiving orally delivered steroid treatment for lymphocytic leukaemia. What makes this study appear quite unique is that demographic data and psychological test responses of patients *and* their parents were correlated with urinary assays (drug concentrations in urine being a measure of compliance). Results indicated that while the rate of compliance was the same for boys and girls, the psychological correlates were very different. Parental personality traits and attitudes were more involved with boy's compliance than with girl's. Parent variables that were positively correlated with compliance in boy's were hostility, anxiety and obsessive-compulsive behaviour. Parents were also more likely to describe compliant boys as vulnerable. Such traits, usually considered to be maladaptive, certainly appeared to facilitate boy's compliance. Parents seemed to have less worry and concern about their daughters and presumably gave them more responsibility for their own medication. This not only provides further evidence for the role of personality in medication adherence, it also raises the issue of a potentially powerful effect of 'secondary' personality characteristics (by virtue of patients' family or carers) on treatment adherence and outcome.

1.3.3.2 Personality, adherence and diabetes mellitus

Gentili et al (2000) have analysed personality traits to study different behaviour in compliance conduct with insulin therapy in Type 2 diabetic patients. Adaptation and coping strategies were also considered. Results revealed that participants who showed more fear, insecurity and initial resistance towards insulin therapy appeared more rigid and conforming in relation to treatment. These individuals also revealed more personality aspects compatible with the presence of passive-aggressive and avoidant traits.

In a study examining the association between 'hardiness' and compliance in elderly patients with diabetes, Ross (1991) discovered that a significant correlation existed between hardiness and compliance variables. This suggests that the degree of hardiness in individuals with diabetes may predict compliance to a prescribed diabetic regimen.

As mentioned, most studies conclude that personality factors are unrelated to adherence to treatment programmes. Although evidence for this appears to be largely unreported in the literature around HIV/AIDS, Hepburn et al (1994) do provide support for this disassociation in relation to diabetes. In a large study of 303 insulin-dependent patients, no significant correlations were observed between personality variables and measures of compliance, either physiological or by patient self-report. Thus, a contradiction is evident in the literature concerning the actual role personality may or may not play in predicting adherence. The vast individual differences between chronic illnesses will most likely ensure that such discrepancies are durable facets of any research into the personality and adherence interaction. Another important feature of this particular study is that it indicates the difficulties in accurately measuring patient adherence to treatment. This concept warrants a fuller critique and will be returned to for further discussion later in this research thesis.

1.3.3.3 Personality, adherence and organ transplantation

Explicit psychological factors and adherence issues are not widely commented on in the literature on solid organ transplantation candidates, and how they are evaluated for treatment. In this contentious aspect of medicine, medical review boards have been established that consider medical, psychosocial, and financial factors in choosing appropriate candidates for transplant surgery. Psychological evaluation can furnish clinically useful baseline data regarding the patient's emotional and cognitive functioning, and identify other individual and familial variables that may affect patient adherence and the outcome of transplantation. Such research, for example by Shapiro et al (1995), has attempted to predict compliancy problems and morbidity

after heart transplantation. Although not explicitly measuring personality characteristics per se, this study evaluated a number of prospective psychosocial risk factors in adult patients undergoing heart transplantation to determine their associations with morbidity, mortality and compliance. Compliance problems and episodes of organ rejection were discovered to be significantly associated with substance abuse history, evidence of personality disorder, and a global measure of psychosocial risk. Survival was not associated with any of the predictor variables. Research like this suggests that an evaluation of broader psychosocial factors can help identify patients at increased risk of issues of problematic compliance. Therefore, while pure personality characteristics in isolation may not reliably predict poor adherence (see Hepburn et al, 1994), widening the area of measurement to consider a possible interaction with psychosocial factors may be a prudent inclusion to research into adherence and life-threatening illness.

Unfortunately, as in HIV, there has not been any systematic and comprehensive review of the literature on personality-driven predictors of non-adherence in organ transplant patients thus far. Non-adherence impairs both quality of life and life span as it is a major risk factor for graft rejection episodes and is responsible for many deaths after the initial recovery period. Therefore, to best select potential organ recipients, it would appear to be the ideal that patients who are very likely to show non-compliant behaviour could be identified already before receiving organ transplants. For a literature overview demonstrating the necessity of pre-operative psychosocial screening regarding predictors for post-transplant compliance, the reader is directed to Bunzel and Laederach-Hofmann (2000).

1.3.3.4 Personality, adherence and renal failure

Studies into renal failure and haemodialysis adherence have arguably received most interest from psychologically-minded clinicians, as the author observes the introduction of psychological models of personality into the literature research base of this field of psychological medicine. By applying the Five-Factor Model of

Personality[6], various studies (for example: Christensen and Smith, 1995; Moran et al, 1997; Weibe & Christensen, 1997) have sought to identify personality correlates of adherence and health outcomes. The research has shown that in general, health beliefs and, more specifically, traits of conscientiousness, interact to predict physiological measures of medication adherence. However, findings have also suggested that an interaction of high conscientiousness and high perceived severity of illness was associated with poorer patient adherence.

Vives et al (1999) examined the impact of social-clinical factors over personality dimensions. They also sought empirical evidence of the relationship between internal locus of control experience and higher levels of treatment adherence in patients with renal failure. The impact of socio-demographic and clinical factors showed no significant statistical differences with regard to treatment adherence, health perception and the dimensions of personality. They found no statistically significant association between the dimensions of personality and adherence. However, there was a tendency to correlate the dimension of locus of internal control with adherence to treatment. The results of this study may be somewhat misleading as a health locus of control scale[7] constituted the only actual measure of personality. The study therefore raises issues around how to measure not only adherence, but also personality in a medical sample. Reliable measurement of these variables shall be returned to for further discussion later in Chapter 2.

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[6] The Five-Factor Model of Personality (McCrae and John, 1992) – There is increasing recognition of the utility of the five-factor taxonomy in elucidating personality correlates of health-related outcomes. One such application is the usefulness of five factor personality measurement in understanding patient adherence to a prescribed medical regimen. A conceptual examination of the five-factor taxonomy suggests that Dimension III, labeled Conscientiousness, by Costa & McCrae (1992), may be the most accurate trait descriptor of those qualities of the individual thought to be important in terms of adherence behaviour. The Conscientiousness factor has been interpreted as 'will to achieve', 'dependability' and 'self-control' by various five-factor theorists (Digman, 1990). The dimension reflects a highly purposeful, well organized and self-disciplined style. It has been suggested that level of conscientiousness in childhood predicts survival in middle to old age (Friedman et al., 1993). The mechanisms underlying this association could not be determined. However, individual differences in health-related behaviours, including adherence, are one plausible mediator of the relationship between conscientiousness and survival.

[7] The Vives et al (1999) study applied Wallston's Multidimensional Health locus of control scale as the only measure of personality. It measures across three dimensions: 1) Internal locus of control, which evaluates the belief that one can control one's own health, 2) Power locus of control, which evaluates the belief that one's own health is controlled by the environment, and 3) Locus of control due to chance, which evaluates the belief that one's health depends on factors absolutely beyond control. As an application of locus of control in adherence research, their results are interesting. However, the measures employed would not appear to constitute a thorough analysis of personality dimensions per se. The expected aims of the study (i.e., an analysis of personality and adherence in renal failure) should perhaps be interpreted with caution.

1.3.3.5 Personality, adherence and severe mental illness

Factors associated with non-compliance with outpatient visits to psychiatric services have also been addressed in a number of studies. Centorrino et al (2001) found significantly higher visit adherence among patients in an acute stage of illness, when the visit entailed psychotherapy rather than pharmacotherapy, and when patients had a personality disorder. Similarly, Matas, Staley, and Griffin (1992), in a thirty-month review of outpatient psychiatry referrals, constructed a profile of the typical non-adherent patient with some similar findings. Significant differences between compliant and non-compliant patients were examined in a sample of 874 referrals. Non-compliant patients comprised 18% of the sample and were significantly more likely to be single, male, previously unmarried, unemployed, and diagnosed with substance abuse or personality disorder.

Poor adherence with long-term antidepressant medication has also been associated with a sensation-seeking personality (Ekselius, Bengtsson and von Knorring, 2000), although it is noteworthy that this study also acknowledges the need for improved methods in ascertaining actual level of adherence among patients.

1.3.3.6 Personality, adherence and life-threatening illness - a research summary

The above examples of research into the interaction between personality factors and adherence to treatment regimens have been discussed in order to present the salience of the problem across a wide range of chronic and life-threatening conditions. The influence of personality and adherence variables span across a broader range of medical and psychiatric circumstances. Examples are too numerous to mention within the confines of this thesis, however the author can direct the interested reader to applied research into adherence in areas ranging across cardiac rehabilitation (Hershberger, Robertson and Markert, 1999; Sromberg, Brostrom, Dahlstrom and

Fridlund, 1999), cystic fibrosis[8] (Geiss et al, 1992), asthma (Haida, Ito, Makino and Miyatrioto, 1995), and maternal phenylketonuria[9] (Waisbren, Hamilton, St.James, Shiloh, 1995). As would be expected, research is also widespread among non life-threatening conditions outside pure medicine, for example, in orthodontics (Sergl, Klages and Zentner, 2000) and opthalmology (Bennet, et al, 1998).

In summarising the general themes within the literature around demographic, psychosocial and explicit personality variables, and their association with treatment adherence in life-threatening illness, a number of tentative conclusions can be drawn. The research allows us to argue that a therapeutic level of adherence is associated with various psychological features, including: a positive adjustment to, and acceptance of, an illness, positive coping strategies, increased self-efficacy, functional levels of anxiety, positive health beliefs, conscientiousness, internal locus of control and general 'hardiness'. Non therapeutic levels of adherence can be associated with the inverse perspective of the above factors, and various under-researched, explicit personality variables such as hostility, sensation-seeking traits, and pathological extremes of personality, including personality disorder. Substance abuse also appears to feature highly in non-therapeutic adherence along with socio-demographic variables such as being single, living alone, poor social support and unemployment.

A review of the literature has also indicated the increasing attempts to apply theoretical models of personality to the research into adherence. This more scientifically robust approach may have arise from the contradictory, and unsatisfactory, results of the earlier research studies examining the influence of personality on regimen adherence. The research base described thus far, highlights

[8] Cystic fibrosis – A hereditary disorder of the exocrine glands. Infection affects mucus-producing glands. It is marked by production of very thick mucus, excess sweating (with loss of electrolytes), and an overactive nervous system. Treatment consists of dietary regimens and antibiotic medication.

[9] Pnenylketonuria (PKU) – An inherited disorder in which the enzyme that breaks down the amino acid pnenylalanine is defective. Build up of phenylalanine in the body leads to central nervous system damage and learning disabilities. Treatment is by special dietary regimens.

the results of studies around well-established life-threatening illnesses and conditions. It also informs us that personality is a relatively recent avenue for scrutiny among those with an interest in improving treatment adherence in a range of illnesses. It is therefore no surprise to discover that a considerable paucity of comment exists in the application of this research to the comparatively new disease that is HIV/AIDS. Relative to the other conditions described above, and given the particularly crucial role of adherence in the long-term success of antiretroviral therapy, not to mention the scale of the HIV epidemic, it appears obvious that researchers should concentrate more effort on studying predictors of non-adherence to HIV therapy. A review of the limited literature that already exists in relation to psychological, and explicitly personality, variables influencing adherence to antiretroviral therapy, follows in the next section.

1.3.4 Demographic, psychosocial, and personality variables influencing adherence to antiretroviral therapy – a review of the literature

A review of the literature surrounding personality factors and their influence on adherence in life-threatening illness, has shown that much research has been conducted producing often contradicting results. Some studies have shown clear associations between personality concepts and adherence while others have not. Relative to other life-threatening illnesses, studies on psychological predictors of adherence in HIV are limited. Even less examined is the specific potential interaction of personality variables with adherence to antiretroviral therapy. [The reader is re-directed to Table 2. for a summary of this research and salient findings]

From a review of the literature reflecting current thinking in adherence to combination therapies, there is an explicit and universal conviction that, for therapeutic success on antiretroviral therapy, viral suppression must be achieved and sustained over time. This implies that individuals must maintain low viral loads through good, if not perfect, adherence. Practically, this will require >90% consumption of the prescribed medications. The price to pay for sub-therapeutic

doses will be resistance to HIV antiretrovirals, putting the success of future combination therapies at risk, thus compromising the life of the individual.

A reappraisal of Sherr's (2000) review of the literature surrounding adherence in HIV therapy, reminds us that non-adherence can be understood in terms of four distinct levels of psychological thinking: cognitive models, psychodynamic models, social concepts and personality concepts. Furthermore, adherence research can be practically approached from four perspectives: the patient, the preparation, the provider, and the environment. This section constitutes a review of the limited literature surrounding *personality* concepts and how they affect adherence from the perspective of the *patient*.

1.3.4.1 Demographic and psychosocial variables and adherence to antiretroviral therapy

It has been demonstrated that certain demographic and HIV risk groups have poorer access to therapy [for example, African- Americans (Moore, Stanton, Gopalan and Chaisson, 1994) and injecting drug users (Solomon et al, 1995)]. However, less data is available on the influence of these factors on adherence to HIV therapy. Certain demographic characteristics have been associated with decreased adherence. Gordillo et al (1998) assessed socio-demographic and psychological variables influencing adherence in a large cohort of 366 HIV-infected individuals. They report unsatisfactory adherence is significantly more common among younger individuals (<32 years old), whereas the best adherence rates are observed in individuals aged between 32 and 35 years old. Intravenous drug users and those below 23 years of age had the poorest compliance with the prescribed treatment. A recent study (Catz, Heckman, Kochman and DiMarco, 2001) addressed the specific difficulties faced by older adults (mean age = 53.4 years) with HIV infection. Less education, poorer relationships with physicians, greater alcohol use and higher levels of somatisation uniquely predicted adherence problems in this cohort.

In another study of HIV-infected individuals, it was observed that women miss a higher percentage of clinic visits than men (Kissinger et al, 1995). They concluded that women may face particular gender-specific barriers to treatment such as finding childcare facilities. Homosexuals and heterosexuals appear to demonstrate similar adherence rates, and those with a lower socioeconomic status are typically less adherent. The specific components of lower socioeconomic status associated with adherence are unstable or poor housing, low income, low level of education, and (in the U.S.) a lack of medical insurance (Coons et al., 1994; Singh et al., 1994). Having a job is also associated with better compliance, as is the perception of a good social support (Gordillo et al., 1998).

Poor social relationships and activities have been associated with lower adherence. Kissinger et al. (1995) speculated that HIV infection is a potential cause of social isolation. Social isolation may therefore be thought of as a risk factor for decreased compliance in HIV-infected individuals.

1.3.4.2 Psychological variables and adherence to antiretroviral therapy

The presence of a psychiatric illness is commonly associated with decreased adherence in patients with mental illness, elderly status, and HIV infection (Broers, Morabia and Hirschel, 1994; Carney, Freedland, Eisen, Rich and Jaffe, 1995; Coons et al., 1994). In a prospective study of HIV-infected individuals, adherent patients (defined as ≥80% adherence) had significantly less depression than non-adherent patients (Singh et al., 1994). In another large study (Broers et al, 1994), 81% adherence was observed in those without psychiatric diagnoses, compared with 53% adherence in those with a psychiatric disorder. Depression is the most commonly cited psychiatric problem among HIV-infected individuals, with prevalence rates ranging from 17-30% (Fernandez and Ruiz, 1989).

Patient attitudes and beliefs related to decreased adherence have been found to include acceptance or perception of the disease, and perceived lack of benefit of treatment (Samel, Libman and Steger, 1992). Similarly, a belief that antiretrovirals

prolong life is strongly associated with increased adherence. These beliefs can also be risk factors among patients with other types of chronic illness. A study by Catz et al. (2001) surveyed patients' own perceptions of barriers to treatment on HAART regimens. The most frequently reported barriers to adherence reflected general concerns about treatment as a reminder of one's HIV status, not wanting other people to know one's HIV status, and difficulty remembering to ask one's health care provider questions about treatment. Consistent with adherence findings in other chronic diseases, depression, severity of side-effects, perceived self-efficacy to adhere to antiretroviral regimens, and social support were each related to adherence in univariate statistical analyses. In mulitvariate analysis, social support and treatment self-efficacy predicted non-adherence. Participants who perceived less emotional support and those who were less confident of their ability to adhere, were most likely to report inconsistent use of HAART. This study, along with that by Gordillo et al (1999), appear to have been the only recent investigations into psychological influences (specifically patient beliefs and perceptions) on adherence in HIV. Few studies of people living with antiretroviral therapy have emphasised the patients' perception of their illness and medication, their understanding of the rationale for treatment and the patient-doctor relationship. Most of the remaining studies in this particular area have exclusively concentrated on socio-demographic data and characteristics of the actual medication. Other life-threatening illnesses, such as those already discussed, have received considerably more attention in relation to psychological determinants of treatment adherence.

Considering that psychological factors per se, have received little investigation in relation to adherence and antiretroviral therapy, it comes as little surprise to learn that personality characteristics and their interaction with adherence ability have not yet been explicitly examined in the context of HIV. However, if adherence is related to the personal ability and willingness to take complex antiretroviral regimens correctly, there is no doubt that personality variables should play an important role. Given the extent of the research into how personality characteristics may place

individuals at risk of becoming HIV infected[10] (refer to: *1.3.2 The role of personality in HIV risk behaviour*), it is even more surprising to discover the paucity of research into how particular personality characteristics may reduce ability to adhere to the demanding drug regimens of antiretroviral therapy.

The following study aims to address some of the absences in the literature surrounding the role of personality characteristics in predicting non-adherence to antiretroviral therapy. The existing research base in personality, adherence and other life-threatening illnesses can inform research questions in the area of HIV.

[10] Prevalence rates of personality disorders among HIV-infected (19-36%) and HIV at-risk (15-29%) individuals are high and significantly exceed rates found in the general population (10%) [Jacobsberg, et al., 1995; Johnson et al, 1995; Perkins, et al, 1993; Weisman, 1993]. Antisocial personality disorder is the most common and is a risk factor for HIV infection. Individuals with personality disorder, particularly antisocial personality disorder, have high rates of substance abuse and are more likely to inject drugs and share injecting equipment compared with those without an Axis II diagnosis [Brooner, et al., 1993; Dinwiddie, 1996]. Approximately half of intravenous drug users meet criteria for a diagnosis antisocial personality disorder [Kleinman, et al., 1994]. Antisocial personality disorder individuals are also more likely to have higher numbers of lifetime sexual partners, to engage in unprotected anal sex, and contract sexually transmitted infections compared with individuals without antisocial personality disorder [Ramrakha et al., 2000].

1.4 Research question & statement of hypothesis

1.4.1 General research question

What are the overall general profiles of *adherent* and *non-adherent* HIV-infected individuals receiving antiretroviral therapy in terms of:

i) general personality characteristics?

ii) attitudes to their illness and healthcare?

1.4.2 Specific research hypothesis

Therapeutic and non-therapeutic levels of regimen adherence to HIV antiretroviral therapy are associated with:

i) personality style

ii) coping styles

iii) attitudes to, and beliefs about, healthcare for HIV illness

iv) treatment prognostic indicators

2 Methods

Before commencement of the study a research protocol was submitted for ethical approval by the Lothian Research Ethics Committee, Edinburgh. The research was granted ethical approval by the Psychiatry/Clinical Psychology Research Ethics Sub-Committee on 12 April 2002. Please refer to Appendix I for a summary of this process including relevant correspondence between the researcher and ethics committee.

2.1 Participants

Participants were recruited from an out-patient Regional Infectious Diseases Unit (RIDU), and an out-patient Genito-Urinary Medicine (GUM) clinic in the Lothian region. In-patients at the RIDU were also invited to participate in the study. All participants who were at least 18 years old with an HIV positive status, and in receipt of antiretroviral therapy for the duration of a three month period (from 1st January 2002 until 30th March 2002), were considered eligible for this study. Participants were recruited during March, April and May 2002. HAART patients are asked to attend regular appointments to monitor their progress on treatment regimens. The frequency of these appointments varies from patient to patient. The three month recruitment period was therefore imposed in order to reach all eligible patients with information about the study. It also ensured that adequate time had elapsed to allow the medication to have a measurable impact on physiological variables, and to enable later comparisons of theses measures between 'good' and 'poor' adherers. Participants with gross cognitive deficits were ineligible (for example problems with vision or memory caused by HIV infection or opportunistic infection of the central nervous system or eyes).

A total of 320 patients were offered information about the research (see Appendix Ic: Patient Information Sheet). Of this population, 240 were in attendance at the

RIDU and 80 were patients attending GUM. Patients were identified as eligible for the study from a printed database record of patients of both clinics. Anonymous, sealed envelopes, each containing a patient information sheet, participant consent form and return envelope, were distributed to reception staff at the RIDU and GUM clinic. Reception staff at each clinic were also given a printed list of eligible patients due to attend their particular department over the 3 month recruitment period. On arrival for their appointments, patients were offered a sealed information pack and asked to consider whether or not they wished to participate. Of the 320 eligible persons on HAART regimens who were approached, only 26 (8%) agreed to participate, and 16% of patients declined the offer to receive information. Most individuals approached but not recruited indicated that they did not have the time to participate or were not interested in doing so.

2.2 Procedure

Once patients had read the information provided about the study, and following the provision of written informed consent (refer to Appendix Id: research participant consent form), patients were contacted by letter or phone and were scheduled appointments for individual interview sessions to complete a battery of questionnaires within 3 weeks of their recruitment at medical departments. Participants were scheduled appointments to meet with the researcher between April and July 2002. Participants were seen at either the RIDU (to coincide with their next medical consultation) or at the premises of the Community HIV Service. Two participants were visited at home as it was inconvenient for them to travel. One participant was seen on the RIDU in-patient ward due to a deterioration in health.

All participants were invited to re-read the patient information sheet and any queries were answered at the outset of each appointment. A brief outline of the research objectives was verbally presented to each participant.

All measures were administered using a semi-structured interview format in order to minimize the duration of appointments. The length of appointments ranged from 50 minutes to 110 minutes. Each participant was interviewed once. The researcher was present for the duration of all appointments should participants require assistance in their completion of measures. Once completed, each participant and their completed measure were allocated a unique participant identification number. This ensured participant anonymity and enabled completed measures to be cross-referenced for the analysis. Participant information and completed measures were, at all other times, stored in a locked filing cabinet to ensure full confidentiality of research materials.

2.3 Measures

The following measures were administered to each participant:

2.3.1 Socio-demographic and adherence self-report assessment

A specific questionnaire was constructed for use in the study in order to collect data on socio-demographic information, and the participants' self-report of their own level of adherence and associated difficulties (for a sample copy of this data collection questionnaire please refer to Appendix II: Socio-demographic and adherence self-report questionnaire).

2.3.1.1 Socio-demographic data

Socio-demographic data included: gender, date of birth, age, employment status, sexual orientation, marital status, route of HIV infection, date of HIV diagnosis, AIDS diagnosis status, history of illegal drug use, alcohol use, and prescription drug use. The socio-demographic data allowed the production of descriptive statistics regarding the sample population.

2.3.1.2 Adherence self-report data

The adherence section of the questionnaire was designed to both elicit specific information concerning current antiretroviral medication, and guide a more informal discussion of adherence issues particular to each individual. The questionnaire assisted data collection regarding: knowledge of CD4 count and viral load, knowledge of drug resistance, current antiretroviral regimens, previous gaps in therapy, frequency of missed or delayed doses, reasons for missed or delayed doses, drug side-effects, and personal general comments about combination therapy.

The adherence section of the questionnaire asked participants to indicate the number of antiretroviral medication pills in their prescribed regimen that they had missed over the previous 3 months. A short to medium-term pattern of medication adherence could then be assessed. From the data, calculation indicated whether participants reported perfect adherence or could be classified as missing doses on a daily, weekly or monthly basis during the 3-month period.

2.3.2 Psychological (personality) assessment

Two distinct psychological assessment instruments were used to elicit information on participants' personality styles and a range of psychological factors affecting the course of participants' medical treatment for HIV. Both are grounded in a biopsychosocial theory of personality developed by Theodore Millon (Millon, 1983). The assessments are from a range of measures commonly referred to as 'the millon inventories'.

2.3.2.1 Millon Index of Personality Styles (MIPS)

The Millon Index of Personality Styles (Millon, Weiss, Millon and Davis, 1994) was chosen to examine personality style. The MIPS is a 180-item, true/false questionnaire (Appendix III: MIPS test booklet), designed to measure personality styles of normal and reasonably functioning adults between the ages of 18 and 65+ years. Items were endorsed by respondents on a separate answer sheet (Appendix IV:

MIPS answer sheet). The MIPS consists of 24 scales grouped into 12 pairs. Each pair contains two juxtaposed scales. For example, the 'Retiring' and 'Outgoing' scales are considered a pair.

As Table 4 shows, the 12 pairs of MIPS scales are organised into three major areas: Motivating Aims, Cognitive Modes, and Interpersonal Behaviours. The 'Motivating Aims' sub-scale assesses an individual's orientation toward obtaining reinforcement from the environment. The 'Cognitive Modes' sub-scale examines styles of information processing. The 'Interpersonal Behaviours' sub-scale considers on-going social roles and relationships and includes variations on the factors used in the five-factor model (Tupes and Christal, 1992). In addition to the 12 pairs of content scales, the MIPS contains three validity indicators: Positive Impression, Negative Impression, and Consistency. The MIPS also contains a composite of overall psychological adjustment called the Adjustment Index.

Table 4: Organisation of the MIPS Scales

Validity indicators	**Motivating Aims**	**Cognitive Modes**	**Interpersonal Behaviours**
Consistency	Enhancing	Extraversing	Retiring
Positive Impression	Preserving	Introversing	Outgoing
Negative Impression	Modifying	Sensing	Hesitating
	Accommodating	Intuiting	Asserting
	Individuating	Thinking	Dissenting
	Nurturing	Feeling	Conforming
		Systematizing	Yielding
		Innovating	Controlling
			Complaining
			Agreeing

The MIPS is usefully applied to settings in which clinicians seek to identify, understand, and assist normally functioning adults. The scale measures normal

personality style, not clinical disorders, and has a rich theoretical foundation in a model of personality that is deeply rooted in a biopsychosocial theory (Millon, 1969/1983; 1990;1991). The MIPS was selected as the most appropriate measure of personality for this study, firstly because, along with the MBMD (the second psychological measure in this study), it is intrinsically linked to a sound theoretical model of personality.

The five-factor model of personality has recently often been used in elucidating personality correlates of health-related outcomes (Smith and Williams, 1992). However, the five-factor model is largely devoid of theory, having its roots in the statistical analysis of lists of adjectives used by ordinary people to describe others (Goldberg, 1993). Nonetheless, validity[11] for both models is reinforced by the finding that the MIPS appears to factor into five dimensions that are consistent with the five-factor model of personality (Millon, 1997). This finding is important because of the parallels between the theoretically derived MIPS scales and the empirically derived five-factor model. The decision to use a theoretically based model of personality is summed up by a quote from Weiss who argues that,

"..... future research on the five-factor model should seek to place that model into the larger nomological network of established personality theories to further our understanding of the structure of normal personality."

(Weiss L.G., 1997)

The second reason for choosing the MIPS was the fact that it is quick to administer; an important consideration which allowed potentially richer information to be elicited from the informal semi-structured adherence interview. The length of time

[11] The MIPS scales have been validated against other measures of similar personality styles and constructs. Such data are presented in the MIPS technical manual (Millon et al., 1994) in the form of correlations with six widely used personality measures and one measure of depression.
Internal consistency and test-retest reliability of MIPS scales has been found to be very good. Median split-half reliabilities were r = .82 and r = .80 for an adult and college sample, respectively. Test-retest stability over 2 months was estimated in samples of 50 adults and 110 college students. Correlations corrected for variability of scale scores at first testing ranged from .73 to .91 in the adult sample (median = .85) and .78 to .90 in the college sample (median = .84) [Millon et al., 1994].

spent interviewing each participant varied considerably therefore quickly administered psychometric assessments were essential. The MIPS was predominantly applied to participants in order to examine hypothesis 2.

2.3.2.2 Millon Behavioural Medicine Diagnostic (MBMD)

The Millon Behavioural Medicine Diagnostic (Millon, Antoni, Millon, Meagher and Grossman, 2001) is a substantially up-graded version of the Millon Behavioural Health Inventory or MBHI (Millon, Green and Meagher, 1979/1982). Both inventories were designed to,

".....provide the critical psychological information doctors need to treat the whole patient."

(Millon T. et al., 2001)

The MBMD (Appendices V & VI: MBMD test booklet and answer sheet) is a 165-item, self-report inventory with 29 Clinical scales, three Response Patterns scales, one validity indicator, and six Negative Health Habits indicators. It is designed to assess psychological factors that can influence the course of treatment of medically ill patients. The MBMD was developed in consultation with doctors, psychologists, nurses and other health professionals who work with the physically ill. As a result, it reflects issues that are relevant to a thorough understanding of the attitudes, behaviour and concerns of medical patients. The inventory was developed for use in clinical practice, hospitals, outpatient settings and in research. It is especially useful when applied to patients in which psychosocial factors may play a role in the course of disease and treatment outcome.

The MBMD assesses several important psychosocial characteristics that the MBHI does not provide explicit information on. These include information about:

- the presence of psychiatric indicators that may influence patients' adjustment to their medical condition

- coping styles that reflect recently derived personality disorders (Millon and Davis, 1996)
- psychological factors related to cognitive appraisals (e.g., self-esteem and general efficacy), resources (e.g., spiritual and religious), and contextual factors (e.g., functional abilities)
- lifestyle behaviour (e.g., alcohol and substance abuse, eating patterns, inactivity and exercise)
- patients' communication styles (tendency toward disclosure, social desirability, and devaluation)
- predicting patient adherence, medication abuse, and use of medical services, which can be useful for healthcare management decisions and triaging mental health treatment

Since the development of the MBHI in 1982, numerous clinical studies in diverse hospital settings have shown that patients who receive cognitive-behavioural interventions require fewer medical services than those who receive standard care. Research informed interventions can reduce healthcare costs significantly and ultimately enhance patient adherence to treatment regimens. This research has included the use of the MBHI and MBMD in studying adjustment and health behaviour in straight, gay and bisexual populations of men and women living with HIV (Antoni and Emmelkemp, 1995; Byrnes-Pereira, Antonio, Davidson and Simon, 2000; Starr et al., 1996).

Given the HIV specific research base, and the inclusion of scales assessing coping styles and issues of adherence, the MBMD was therefore chosen as an appropriate measure for examining the hypothesis. Like the MIPS, the MBMD is also easy and quick to administer. Fundamentally, both measures are derived and developed from the same theory of personality, making comparisons of results particularly meaningful, and especially in a theoretical context. This was viewed a sensible

approach to the research question, and is given emphasis by a quote from a review article on patient adherence and chronic illness by Wiebe and Christensen,

"……research has examined the utility of using standardized personality inventories as predictors of adherence……however, many of these studies have not been theoretically driven and have lacked an organizing framework to guide measurement attempts."

(Wiebe J.S. and Christensen A.J., 1997)

The reader is referred to Appendices VII & VIII for full descriptions of the MIPS and MBMD scales. All MIPS scales were used in the research. Not all MBMD scales were considered necessary to apply within the assessments (for example those assessing negative health habits such as smoking, lack of exercise and diet). The focus of the study remained on the personality issues surrounding individuals' approach to their healthcare.

2.3.3 Note on adherence assessment

From the introduction to this area of research it is noted that adherence can be assessed in a variety of different ways (refer to *Table 1: Summary of recent studies of adherence to HIV antiretroviral therapy*). For this study three different methods were considered as a measure of patient adherence:

i) Self-report of previous 3-month adherence

ii) Viral load

iii) MBMD Treatment Prognostics Scale – '*Problematic Compliance*'

Upon analysis of the viral load data, it was observed that of the participants who had reported missing any antiretroviral dose in the past 3 months (n=19), only 3 (16%) had detectable viral loads (>400 copies/ml). It became apparent that, given the sample size (N=25), participants could not be classified as 'good' or 'poor' adherers on viral load alone. The Problematic Compliance scale of the MBMD proved to be a

useful post-hoc reference for adherence, but as it was one of the measures acting as an independent variable in the study it was not used to classify adherence per se. In line with the reliability reported in other studies of adherence (please refer to Table 2.), it was therefore decided to apply patient self-report as the primary function of adherence, and it was the main dependent variable in this study. Viral load and the Problematic Compliance indicator will be discussed later in this report.

A review of the literature on research using self-report as an adherence measure (Catz et al., 2000; Gordillo et al., 1999), advised that the cut-off point for determining good or poor adherence should lie between 80-90% adherence. This was a potentially vague boundary, however the inability to use viral load as an adherence measure suggested that 90% was too high a cut-off point. It was felt that the use of the semi-structured interview, which provided the opportunity to carefully probe respondents honest self-report of adherence, would compensate for the loss of viral load indicators. Therefore in line with previous research into medication adherence and life-threatening illness it was decided to refer to an 80% adherence cut-off point. A review of the research also indicated that, in the case of HIV/AIDS, this 80% cut-off corresponds to a reported frequency of missed doses of *>1 dose/week.* This then acted as the boundary for classifying participants as either 'good' or 'poor' adherers upon their self-report of adherence during the semi-structured interview.

3 Results

3.1 Descriptive results analysis

Descriptive statistical analysis was applied to much of the data collected using the demographic and adherence self-report semi-structured interview schedule. The results of this initial analysis are displayed below.

3.1.1 Demographic-related self-report data

A total of 25 participants completed measures. All questionnaires were completed in full with no omissions from the data collected. The sample comprised 16 males (64%) and 9 females (36%) who fell into a variety of age ranges. Such data are presented graphically in Figures: 4 & 5 (pages 78 & 79).

(All frequencies correspond to the number of participants meeting each condition).

Figure 4: Number of individuals by gender

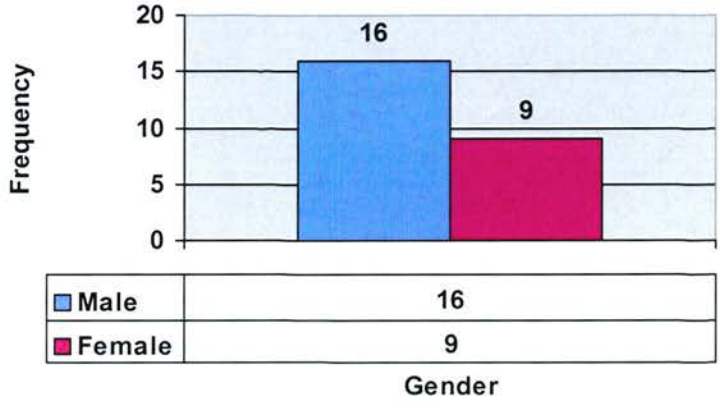
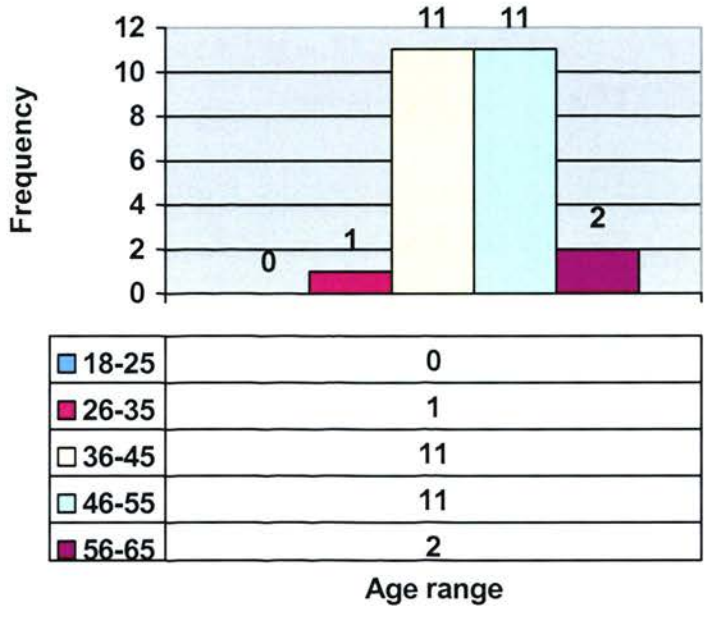


Figure 5: Number of individuals by age range



Data on the following variables are also included in the following charts: marital status, sexual orientation, route of HIV infection, time since diagnosis, and frequency of AIDS diagnosis.

(Of all the participants 56% were single, 20% married, 8% divorced and 16% cohabiting. 56% identified as being heterosexual and 44% as homosexual.)

Figure 6: Number of individuals by marital status

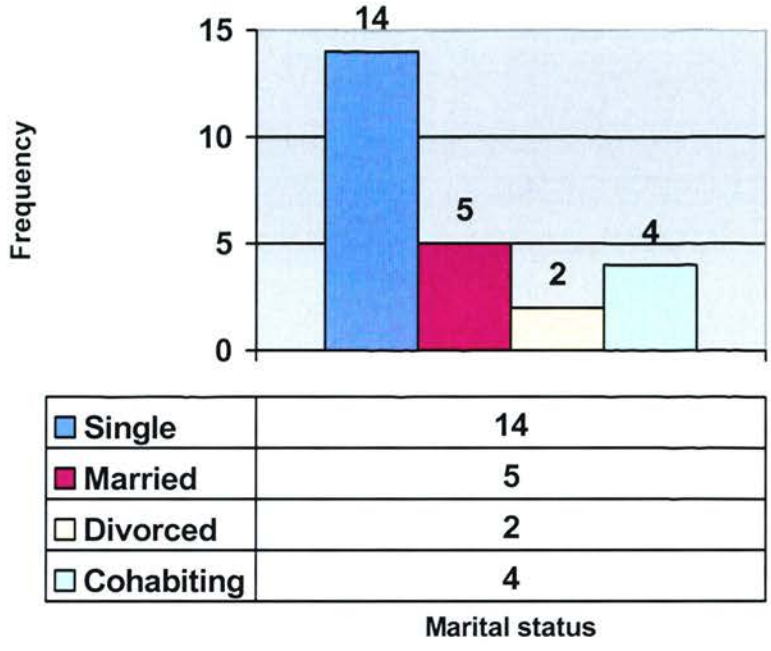
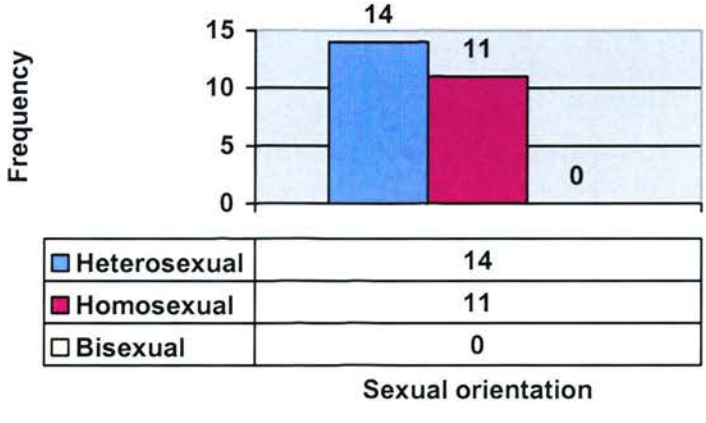


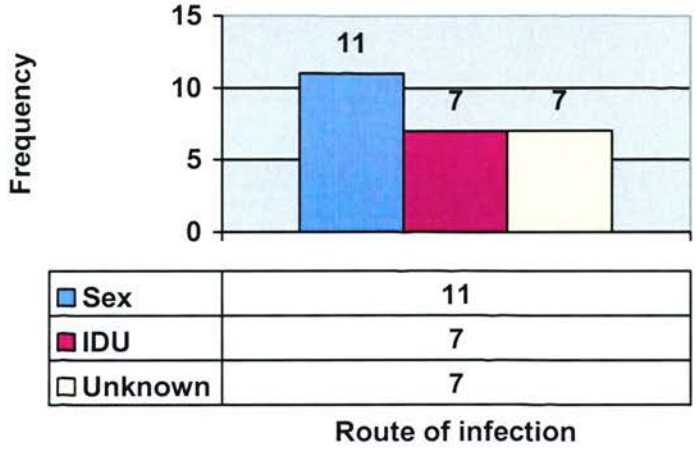
Figure 7: Number of individuals by sexual orientation



A surprisingly high number of individuals in this sample (28%) reported not knowing how they became infected with HIV. In Lothian, out of those currently receiving antiretroviral therapy (458) only 15 individuals are reported as becoming HIV positive through unknown routes. This might suggest that some participants in

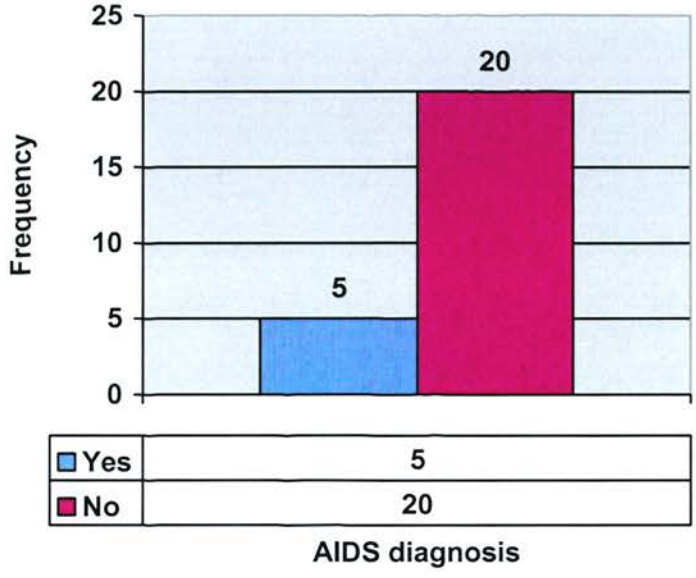
this study were unwilling to disclose their route of infection and chose to give a response of *unknown*.

Figure 8: Number of individuals by route of infection



The semi-structured interview scheduled also included an item on the presence of an AIDS diagnosis. As mentioned earlier, there has been some variation in the exact medical status or series of conditions that are necessary for a diagnosis of AIDS. Before coming to a diagnosis of AIDS, doctors consider a variety of symptoms and tests. There is no single test for AIDS. They may look for one of the opportunistic infections or cancers in the presence of an underlying immune deficiency. Tests may also be carried out to try to seek a positive diagnosis of *pneumocystis carinii,* one of the AIDS-defining illnesses. Five respondents initially reported that they *thought* had previously been diagnosed as having AIDS, but were unsure whether or not their consultant had ever done this, reflecting the ambiguity in the diagnosis. All five individuals (20%) eventually concluded that they had been diagnosed with AIDS at some point and that, as far as they were aware, they still had the diagnosis. Figure 9 (page 82) presents the incidence of AIDS diagnoses within the sample.

Figure 9: Number of individuals by AIDS diagnosis



3.1.2 Adherence-related self report data

The semi-structured interview schedule also permitted the collection of data, by self-report, related to individuals' particular antiretroviral dosing regimens. The interview was designed to obtain an accurate recording of medication factors, and assess to what extent participants were adhering to their particular medication regimen. At some point, all except two of the participants reported that they had experienced significant gaps in their treatment regime. These gaps were often referred to as 'drug holidays', and were all noted taken for at least a duration of three months. Participants' reasons for taking these breaks from treatment were in relation to experiencing adverse side effects to a previous antiretroviral combination. Gaps represented a treatment free period before beginning an altered treatment regimen, hopefully with less disagreeable side effects.

The data related to medication regimens included: time since HIV diagnosis, the number of different antiretrovirals taken per day, and the cumulative number of pills

taken per day. This information is presented below in summary Table 5, reporting means for males and females under each condition.

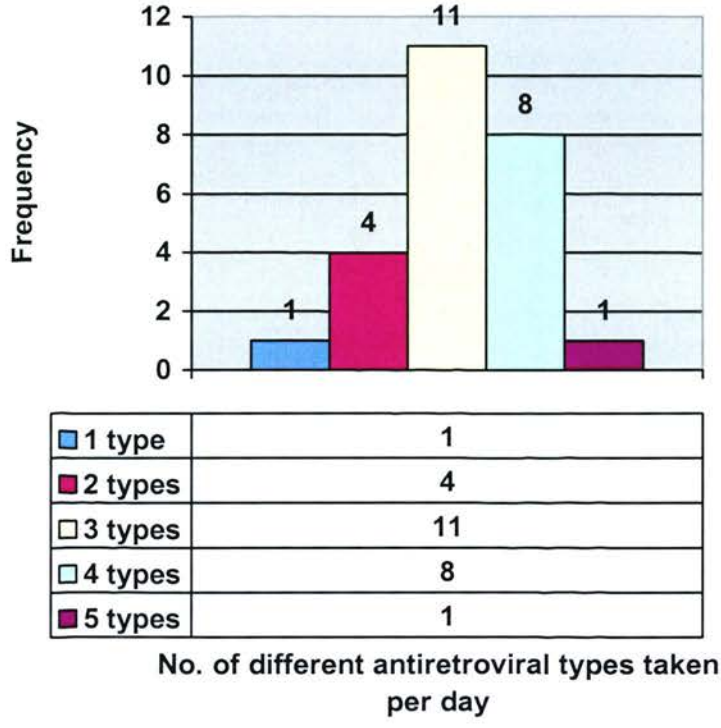
(Once again, all frequencies correspond to the number of participants meeting each condition)

Table 5: Time since HIV diagnosis and number of pills taken per day (Means)

Gender		Age	Time since diagnosis (years)	No. different antiretrovirals per day	Cumulative daily pill count
Male	Mean	42	12.0	3	11
N=16					
Female	Mean	38	13.0	3	9
N=9					
Total	Mean	40	12.5	3	10
	Standard deviation	5.52	*2.41*		

Most participants were taking at least three different antiretrovirals in combination on a daily basis. This would be observed across a wider sample of those on HIV therapy. Advances in drug development and effectiveness have allowed many pills, in the past taken separately, to be combined into one pill for ease of administration. Nevertheless some individuals in this study were taking in excess of more than three different pills in any combination. In addition, four respondents were taking in excess of a cumulative total of 16 pills per day[12]. The frequency of individuals taking different antiretrovirals in each daily combination, and the total number of pills taken, is best demonstrated graphically (please refer to Figures 10 & 11, pages 84 & 85).

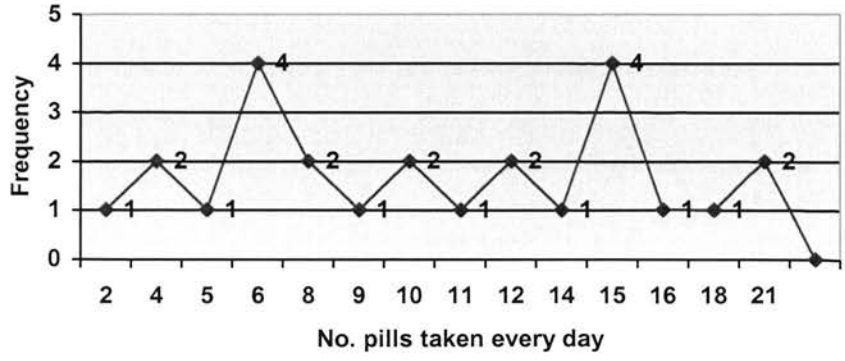
Figure 10: ***Number of individuals by frequency of antiretroviral types in combination taken per day***



The cumulative number of pills taken daily was observed to fluctuate across the individuals sampled.

[12] One participant in the study was on a daily regimen of 15 antiretrovirals. In addition he also took prescription medications for the treatment of HIV-related infections and various other ailments. Medication *outside* his combination therapy consisted of 13 pills per day. The total number of pills taken every day by this individual came to 28.

Figure 11: ***Number of individuals by total number of antiretroviral pills† taken each day***

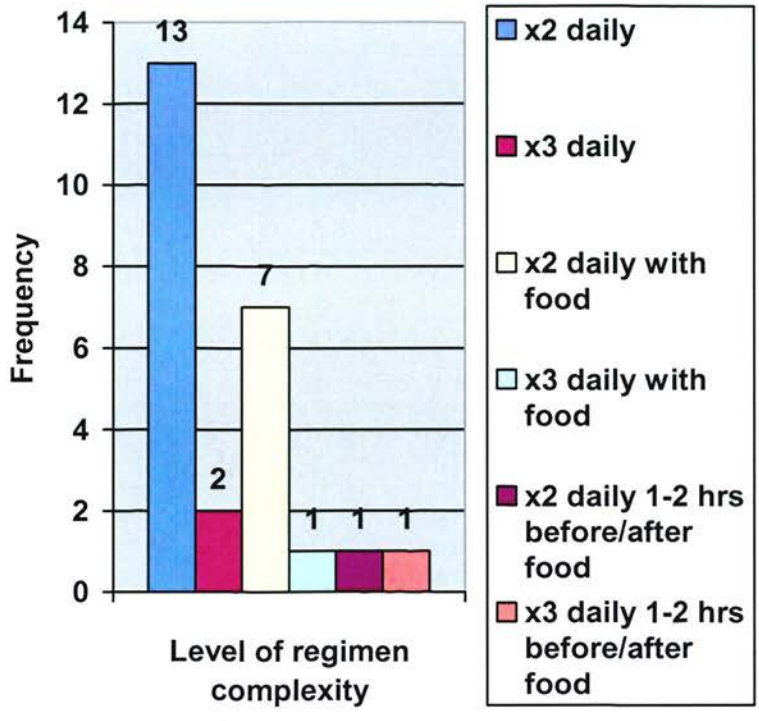


† This total is exclusive of other prescription medications

Despite, as mentioned earlier, the recent medical advances leading to the physical combination of different antiretrovirals into *less* pills, a strong positive correlation *($r=0.694$; $n=25$; $p<0.01$)* was observed between the numbers of different antiretrovirals taken and the cumulative daily pill intake.

Antiretroviral treatments are observed to vary considerably in relation to the complexity of the regimen. Not only are there variations in the number of pills taken by individuals, the time of dosing throughout the day also varies, as does advice from consultants on whether to take pills with or without food. Very often pills not taken with food are instead to be taken between 1-2 hours before or after eating. The regime varies according to the individual circumstances of the medication, the patient and the aetiology of the infection. The analysis included a consideration of the complexity of treatment regimens on adherence. A further examination of the interaction between adherence and regime complexity occurs later in the report, although the frequencies of individuals on any particular level of regimen complexity are detailed in Figure 12 (page 86). The legend indicates the number of pills taken at any one dose and the additional instructions for proper medicating.

Figure 12: Number of individuals by regimen complexity†



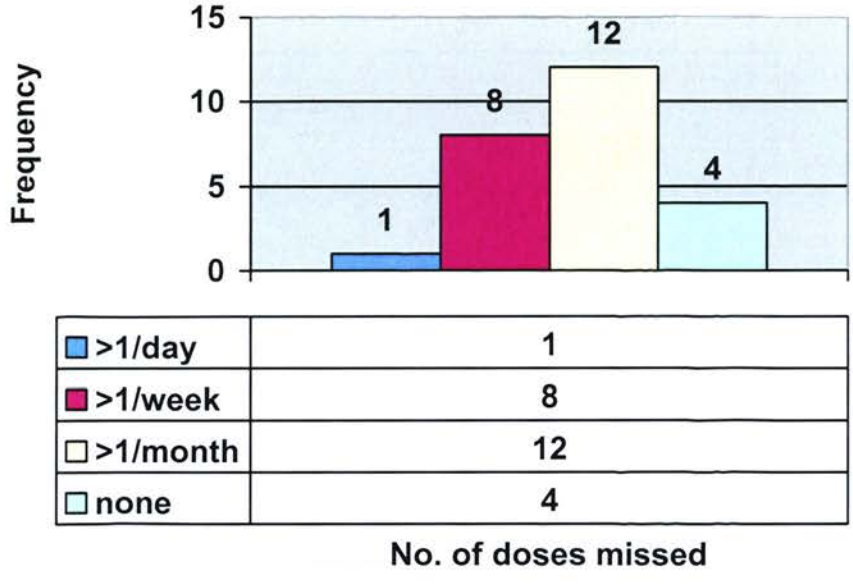
† Graph legend refers to the regimen for any one particular antiretroviral drug. Please note that dosing requirements are repeated for other drugs in the regimen

As can be seen from Figure 12, the majority of respondents were taking a combination of antiretroviral medications within a 'twice daily' treatment regimen. Most individuals receiving HAART in the Lothian region were known to be on a combination of at least three different drugs, therefore in terms of the number of discrete antiretrovirals taken by each individual, this suggested that the participants in this study comprised a representative sample.

Once it was established how the sample presented in terms of level of regimen complexity, information was collated from the interview material to establish the extent to which doses within each individual regimen were missed or not taken according to instruction. Doses were considered as 'missed' if they were not taken at all, and in the case of delayed doses if they were taken outside a time-frame of a ½

hour[13] either side of the specific dosing time of the regimen. For example, on a regimen expecting a combination of antiretrovitals to be taken at 8.00am and again at 8.00pm, the morning dose would be 'missed' if it was actually taken after 8.30pm. The frequency of such occurrences across the sample is displayed in Figure 13.

Figure 13: ***Number of individuals by self-reported number of doses missed over last 3 months***



The self-report of number of missed doses over the previous three months was the basis for the dependent adherence variable. The decision to establish a cut-off point for good and poor adherence was based upon previous research into adherence in HIV therapy *(please refer to methodology)*. Therefore, upon a study of the above chart, the frequencies of individuals who met each condition are to be found in Table 6.

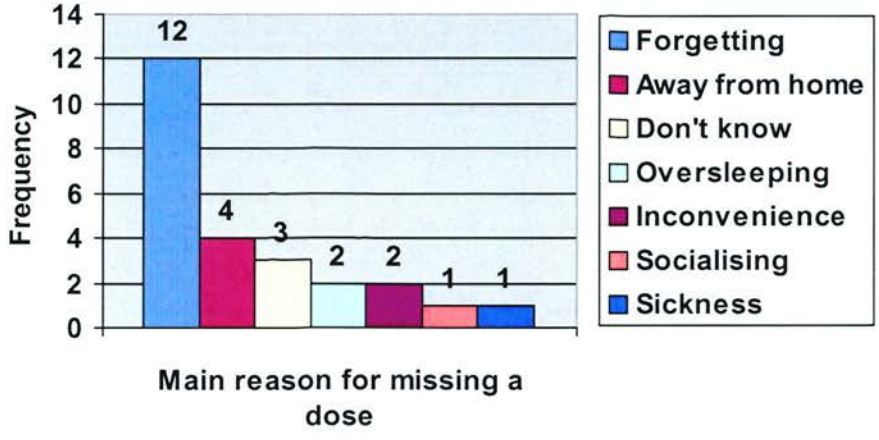
[13] The use of a half-hour parameter either side of the specified dosing time was imposed following a literature review which indicated that previous studies into HIV medication adherence had identified this 'therapeutic window' as the appropriate time to medicate.

Table 6: Number of individuals by categorisation of 'good' and 'poor' adherence

	Good adherence **<1 missed dose per week**	**Poor adherence** **>1 missed dose per week**
No. of participants meeting each condition	16	9

The final part of the adherence section of the semi-structured interview enabled some qualitative information to be gathered concerning the reasons why these doses are occasionally missed (refer to Figure 14, page 90). Participants would typically begin their response by simply stating that they 'don't know' why these doses would have been missed. However the interview process enabled effective probing on this issue and most participants, with the exception of three, were guided towards the identification of discrete, individual explanations for missed or delayed doses. Responses by self-report varied across participants, although a closer inspection of the reasons given allowed each to be grouped under a range of main reasons for missed doses (please refer to Figure 14).

Figure 14: Number of individuals by main reason for missing a dose



Most respondents stated that forgetfulness accounted for the majority of missed doses. Some participants volunteered several different reasons and appeared quite clear about the situations leading to their own experience of missed dosing. It was noted that several participants claimed that, over the last 3 months, they had missed doses through apparent 'laziness'. As one respondent, on an 8.00am/8.00pm dosing time, described,

" I deliberately slept through the alarm, I knew I had to take it [the medication] but I was really tired and just couldn't be bothered getting up……doesn't normally ever happen but I was just so fed up".

This incident was classified as 'inconvenience' as the main reason for the participant missing the dose. Similarly, another respondent reported missing six doses over two days for the following reason,

"I just decided I'd had enough that day……didn't take any that day or the following day……I've been undetectable [viral load] for quite a while and took some time off".

Again, this response was classified as 'inconvenience', although both examples are suggestive of an underlying psychological factor perhaps indicating that these

individuals had almost had enough of meeting the demands of their particular treatment regimen and felt driven to rebel against it.

Demographic results from the semi-structured interview were cross-tabulated with the results self-report adherence measure. The resulting contingency tables were analysed by applying a chi-squared statistic to determine the presence of any association between reported frequencies of occurrence of descriptive demographic or treatment regimen data, and level of regimen adherence. No significant associations were discovered upon this analysis.

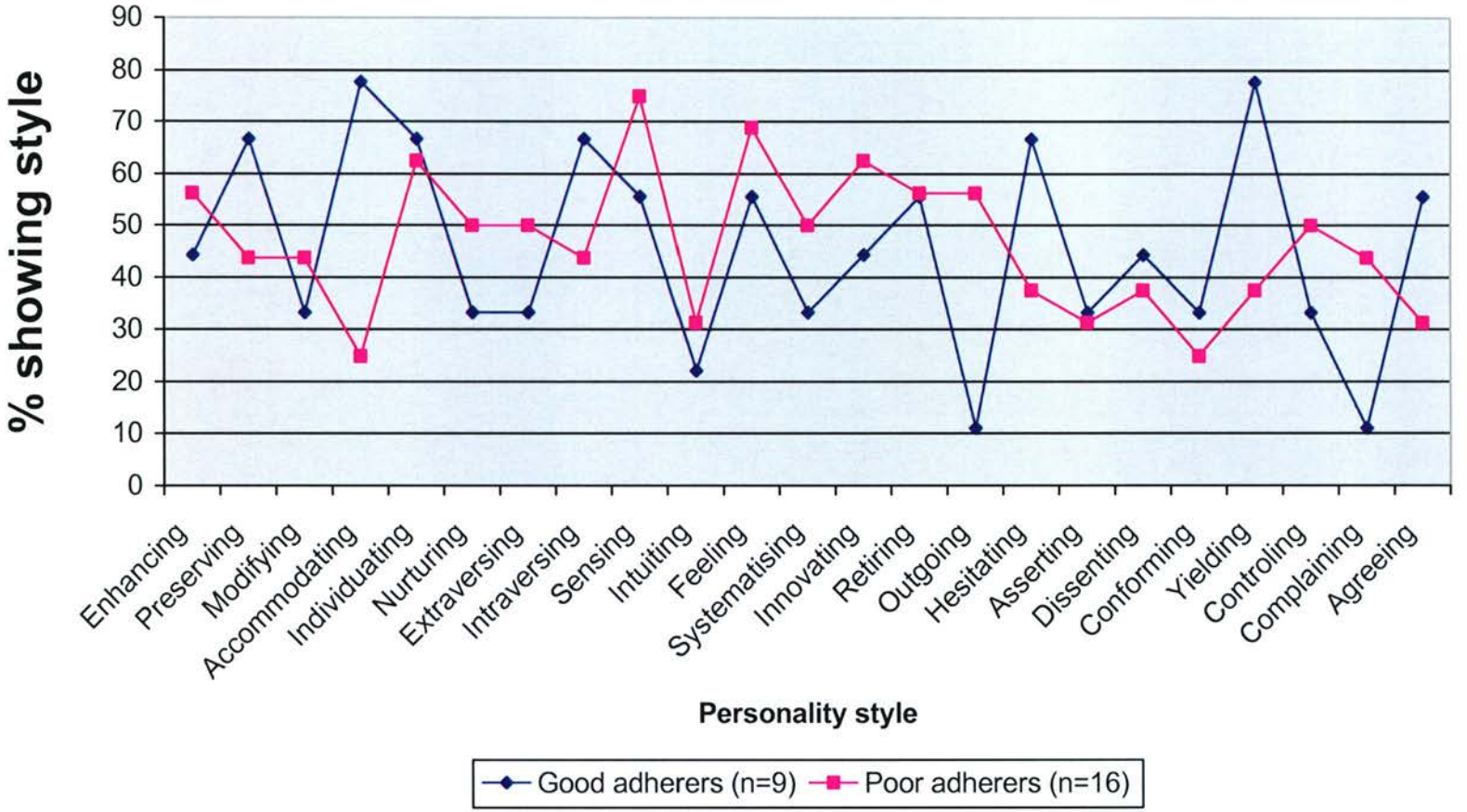
3.1.3 Personality and adherence-related data

By this stage of the investigation, each participant had been categorised as either a 'good' or 'poor' adherer to antiretroviral treatment. Viral load output was returned to in order to establish if any of the self-reported poor adherers demonstrated levels of detectable viral load (>400 copies/ml) in the previous 6 months (February to July 2002). Four individuals within the sample (16%) were noted to have had viral loads >400 copies/ml in the previous 6 months. Previously, an examination of the last 3 months' data had revealed 3 individuals (12%) with elevated viral loads. However, examination of the last 6 months' viral load data was very revealing as 3 out of the 4 individuals with detectable viral load were also identified as poor adherers on the basis of self-report within this study. This finding reinforced the self-reported data of poor adherence as a more reliable function of adherence in general.

Before personality and adherence measures were examined for any meaningful associations between them, the occurrences of the different personality styles among good and poor adherers were considered.

Figure 15 (page 91) is a visual representation of the incidence of each personality style measured by the MIPS across good and poor adherers.

Figure 15: Personality styles observed in good and poor adherers



All personality styles were cross-tabulated with level of adherence. Each resulting contingency table was then subjected to a chi-square (χ^2) statistical analysis to establish any existence of a statistical association between adherence level and personality style. However, as χ^2 does not measure the *strength* of a statistical association, a measure of strength of association for categorical data, the phi coefficient (ϕ), was also applied to the data. The following associations between level of adherence and personality style were discovered:

i) Adherence level and accommodating personality style

Cross-tabulation

			Accommodating No	**Accommodating Yes**	**Total**
Adherence	**Good**	Count	2	7	9
		Expected count	4.7	4.3	9.0
	Poor	Count	11	5	16
		Expected Count	8.3	7.7	16.0
Total		Count	13	12	25
		Expected Count	13.0	12.0	25.0

Chi-Square test

	Value	**Df**	**Significance (2-sided)**
Pearson χ^2	4.996	1	0.025
ϕ	0.447		0.025 (approx. sig)

$\chi^2 = 5.00$; df = 1; $p<0.05$

$\phi = 0.447$; $p<0.05$

It can be concluded that there is a statistical association between adherence and an accommodating personality style. Based on the results, good adherers are statistically more likely to have an accommodating personality style.

ii) Adherence level and systematising personality style

Cross-tabulation

			Systematising No	Systematising Yes	Total
Adherence	**Good**	Count	2	7	9
		Expected count	4.7	4.3	9.0
	Poor	Count	11	5	16
		Expected Count	8.3	7.7	16.0
Total		Count	13	12	25
		Expected Count	13.0	12.0	25.0

Chi-Square test

	Value	Df	Significance (2-sided)
Pearson χ^2	4.996	1	0.025
ϕ	0.447		0.025 (approx. sig)

$\chi^2 = 5.00$; df = 1; $p<0.05$

$\phi = 0.447$; $p<0.05$

It can be concluded that there is a statistical association between adherence and a systematising personality style. Based on the results, good adherers are statistically more likely to have a systematising personality style.

No other statistical associations were discovered between adherence level and personality style. However, the same statistical analysis was conducted across the observed coping styles of the participants. The following significant results were obtained:

iii)Adherence and nonconforming coping style

Cross-tabulation

			Nonconforming No	Nonconforming Yes	Total
Adherence	**Good**	Count	7	2	9
		Expected count	4.0	5.0	9.0
	Poor	Count	4	12	16
		Expected Count	7.0	9.0	16.0
Total		Count	11	14	25
		Expected Count	14.0	11.0	25.0

Chi-Square test

	Value	Df	Significance (2-sided)
Pearson χ^2	6.512	1	0.011
Φ	0.510		0.011 (approx. sig)

$\chi^2 = 6.51$; df = 1; $p<0.05$

$\Phi = 0.510$; $p<0.05$

It can be concluded that there is a statistical association between adherence and a nonconforming coping style. Based on the results, good adherers are statistically less likely to have a nonconforming coping style.

iv) Adherence and forceful coping style

Cross-tabulation

			Forceful No	Forceful Yes	Total
Adherence	**Good**	Count	5	4	9
		Expected count	2.5	6.5	9.0
	Poor	Count	2	14	16
		Expected Count	4.5	11.5	16.0
Total		Count	7	18	25
		Expected Count	7.0	18.0	25.0

Chi-Square test

	Value	Df	Significance (2-sided)
Pearson χ^2	5.30	1	0.021
Φ	0.460		0.021 (approx. sig)

$\chi^2 = 5.30$; df = 1; $p<0.05$

$\Phi = 0.460$; $p<0.05$

It can be concluded that there is a statistical association between adherence and a forceful coping style. Based on the results, good adherers are statistically less likely to have a forceful coping style.

Repeated use of the Chi-Square and Phi coefficient analyses on the relationship between adherence and the Treatment Prognostics scales of the MBMD were carried out. The results were as follows:

v) Adherence and interventional fragility treatment prognostic

Cross-tabulation

			Interventional fragility No	Interventional fragility Yes	Total
Adherence	**Good**	Count	6	3	9
		Expected count	3.6	5.4	9.0
	Poor	Count	4	12	16
		Expected Count	6.4	9.6	16.0
Total		Count	10	15	25
		Expected Count	10.0	15.0	25.0

Chi-Square test

	Value	Df	Significance (2-sided)
Pearson χ^2	4.167	1	0.041
Φ	0.408		0.041 (approx. sig)

$\chi^2 = 4.17$; df = 1; $p<0.05$

$\Phi = 0.41$; $p<0.05$

It can be concluded that there is a statistical association between adherence and the interventional fragility treatment prognostic. Based on the results, good adherers are statistically less likely to have the interventional fragility factor.

vi) Adherence and problematic compliance treatment prognostic

Cross-tabulation

			Problematic compliance No	Problematic compliance Yes	Total
Adherence	**Good**	Count	6	3	9
		Expected count	3.6	5.4	9.0
	Poor	Count	4	12	16
		Expected Count	6.4	9.6	16.0
Total		Count	10	15	25
		Expected Count	10.0	15.0	25.0

Chi-Square test

	Value	Df	Significance (2-sided)
Pearson χ^2	4.167	1	0.041
Φ	0.408		0.041 (approx. sig)

$\chi^2 = 4.17$; df = 1; $p<0.05$

$\Phi = 0.41$; $p<0.05$

It can be concluded that there is a statistical association between adherence and the problematic compliance treatment prognostic. Based on the results, good adherers are statistically less likely to have the problematic compliance factor.

As two treatment prognostic indicators were found to be associated with adherence, an examination was conducted to evaluate any relationship between either of these variables and the treatment regimen variables assessed in the semi-structured interview. Only one association was found to be significant, the interventional fragility indicator and the use of additional prescription medicines by individuals;

vii) Association between interventional fragility treatment prognostic and use of additional prescription medications

Cross-tabulation

		Interventional fragility No	Interventional fragility Yes	Total
Prescription Good	Count	10	10	9
Drugs	Expected count	12.0	8.0	9.0
Poor	Count	5	0	16
	Expected Count	3.0	2.0	16.0
Total	Count	15	10	25
	Expected Count	15.0	10.0	25.0

Chi-Square test

	Value	Df	Significance (2-sided)
Pearson χ^2	4.167	1	0.041
Φ	0.408		0.041 (approx. sig)

$\chi^2 = 4.17$; df = 1; $p<0.05$

$\Phi = 0.41$; $p<0.05$

It is concluded that individuals having to take additional prescription medication as well as antiretroviral treatment, are more likely to express the interventional fragility indicator.

The association discovered between level of adherence and the personality measures was felt to warrant further investigation, in order to assess the presence of significant differences between the means of each measure as they interact with level of adherence. As the data was not normally distributed, as Table 7 (page 99) shows, it was important to select a statistical method that was resistant to skewness. The Mann-Whitney test for independent samples was therefore chosen.

Table 7: Skewness data on personality measures

	Accommodating Personality style	Systematising personality style	Nonconforming coping style	Forceful coping style	Interventional fragility indicator	Problematic compliance indicator
N	25	25	25	25	25	25
Skewness	-.112	-.736	-.383	-.060	-.128	-.595
Standard error of skewness	.464	.464	.464	.464	.464	.464

The original prevalence scores of each individual on each of the measures tested were used in this analysis. The group statistics already demonstrated large differences between group means of good and poor adherence and the personality-defined measures (see Table 9).

Table 8: Group statistics for independent samples test

	Adherence level	N	Mean	Standard deviation	Standard error of mean
Accommodating Personality style	Good	16	45.38	22.71	5.68
	Poor	9	81.89	16.11	5.37
Systematising personality style	Good	16	74.19	15.07	3.77
	Poor	9	27.44	28.85	9.62
Nonconforming coping style	Good	16	39.69	26.40	6.60
	Poor	9	69.89	19.20	6.40
Forceful coping style	Good	16	31.38	29.34	7.34
	Poor	9	59.56	26.81	8.94
Interventional fragility indicator	Good	16	55.13	20.92	5.23
	Poor	9	88.56	20.91	6.97
Problematic compliance indicator	Good	16	53.12	28.37	7.09
	Poor	9	94.00	17.31	5.77

The results of the Mann-Whitney test clearly show that there are statistical differences between the mean scores of good and poor adherers on the personality variables measured. The significance of these results is shown in Table 10.

Table 9: Mann-Whitney test statistics

	Accommodating personality style	Systematising personality style	Nonconforming coping style	Forceful coping style	Intervention fragility indicator	Problematic compliance indicator
Mann-Whitney U	12.000	13.500	23.500	30.500	15.500	12.500
Z	-3.398	-3.315	-2.750	-2.361	-3.200	-3.371
Asymp. Sig (2-tailed)	.001	.001	.006	.018	.001	.001

The results are very significant and it is therefore concluded that good and poor adherers show significant differences based on the following personality-related variables variables:

i) **Accommodating personality style**

Z = 3.40; Significant; p<0.01

ii) **Systematising personality style**

Z = 3.32; Significant; p<0.01

iii) **Nonconforming coping style**

Z = 2.76; Significant; p<0.01

iv) **Forceful coping style**

Z = 2.36; Significant; p<0.05

v) **Interventional fragility treatment prognostic**

Z = 3.20; Significant; p<0.01

vi) **Problematic compliance treatment prognostic**

Z = 3.37; Significant; p<0.01

4 Discussion

This chapter will introduce a discussion of the research findings based upon the hypothesis. The ability of the study to answer the research question will be the fundamental basis of this critique. Consideration as to how the findings of this study fit into the framework set by previous research in this area will also take place. A discussion of the qualitative elements of this research is also thought to be important. Finally, after an examination of the possible limitations to this research, consideration will be given to any implications of the study and the potential for informing current clinical practice and future research in the area of adherence to HIV treatment.

4.1 Comment on demographic data

The semi-structured interview schedule was the only instrument used to collect information on demographic strata across the sample. Despite a considerable amount of potential useful information being collected across several variables it is disappointing that the statistical analysis did not yield any particularly significant findings. However, the frequencies of individuals meeting various conditions of the variables examined, do reflect some of the findings resulting from previous research in this area. Mehta et al. (1997) cite a number of demographic characteristics found to affect adherence with HIV therapy in a review of the literature on the subject. In addition they considered psychosocial/behavioural characteristics, clinical aspects, and healthcare administration and delivery. The Gordillo et al (1999) study identified many variables which were statistically significant predictors of compliance in a univariate analysis. Poorer adherence was commoner among younger individuals with best adherence observed in those aged between 32 and 35 years. Most of the sample used in the research reported here fell within this age range. However, due to the small sample size, inferential statistics could not be applied to analyse for similar findings reported in such previous literature. On first examination of previous research findings, it becomes immediately apparent that their analyses are based

upon research involving considerably larger sample sizes than examined within this study. For example, Gordillo et al. (1999), who were able to produce results based on a sample of 366 subjects. The Gordillo study included an extensive multivariate analysis of the demographic characteristics associated with treatment adherence. They discovered primarily that around three-quarters of their sample were able to be classified as good adherers. A similar finding resulted from this current research study. However, in the research reported in this thesis, no significant associations were observed between adherence and demographic strata. The small number of participants, also meant that a range of investigations could not be reliably conducted, a conclusion reinforced by the fact that responses to the measures did not represent a normal distribution. Many previous studies have enjoyed the advantage of measuring adherence by HIV exposure category as their large response rates allowed for such comparisons. For example, looking for differences between homosexuals, heterosexuals, and within these groups also considering subgroups of individuals who are or are not injecting drug users. Thus, the lack of significant findings in the analysis of adherence by demographic strata in this study could certainly be explained by the very low sample size. Other demographic findings from previous research includes the finding that the male gender is associated with decreased adherence, although many other studies have not found a significant association in this interaction. Some studies, using frequency of appointment-keeping as a measure of adherence, have found that females are less compliant (for example, Kissinger et al., 1995). Many other associated demographic characteristics, which given the sample size could not be accurately researched in this study, would include: level of education, socio-economic status, and perception of social support. It would appear that there are significant associations to be found between adherence and demographic strata. However a reliable examination of them would appear to rely heavily on large sample sizes, and the availability the researcher has in terms of accessing relevant sub-populations based on such factors as employment, risk group, education, and mental health.

4.2 Comment on personality and adherence-related data

The adherence measures provide a basis for a more informing discussion than that surrounding the demographic data. The adherence self-report measure was felt to be a potentially reliable measure of compliance to antiretroviral medication. There are three main reasons for drawing on this conclusion, based upon both the process of data collection and the analysis of objective outcome measures. Firstly, it was observed during the process of meeting with and interviewing participants that perhaps more accurate information regarding their missed doses was being collected tan would have been provided by a straight-forward self-report questionnaire. It is believed the actual interview allowed a productive alliance to develop between the respondent and interviewer, and the dialogue therein enabled open-ended questioning of dosing lapses and regimen difficulties. Such a process would not occur with the use of a self-completed questionnaire, and this may have increased the risk of under-reporting of missed doses. The interview enabled an empathy to develop surrounding the difficulties of treatment adherence and as such was a source of potentially richer information.

The second reason for concluding that this self-report was a reliable avenue of data collection, lies in the finding that the perusal of the physiological measures of viral load indicated that four of the individuals identified as poor adherers via self-report had detectable viral loads in the previous six months. Furthermore, three individuals were demonstrating detectable viral loads in the previous three months. Fluctuations in viral load have been discovered as statistically significant predictors of adherence difficulties in previous studies (for example, Catz et al., 2000). The research reported herein did not establish any statistical validity for the use of the past 3-month measure of self-reported adherence. Furthermore, the decision to ground the good and poor adherence boundary along a cut-off point of >1 missed dose per week, was based upon previous methodology. However, the discovery that detectable viral loads could only be traced to participants in the poor adherence group, suggested that

the adherence cut-off point, and indeed the use of a retrospective 3-month self-report, were appropriate elements in the methodology behind establishing an adherence measure.

Finally, under a post hoc evaluation, it was discovered that one of the treatment prognostic indicators being assessed within the MBMD, was significantly and strongly associated with adherence. Although five other independent variables were also found to be statistically significant with adherence, the fact that this scale '*problematic compliance*', was designed to elucidate patients' disinclination to follow medical advice such as adherence instructions, indicates that the measure of adherence used in this study was reliable.

The finding that a positive correlation was discovered between the numbers of different antiretroviral types taken, and the cumulative daily intake of pills, can be approached as a reasonably obvious, and therefore expected, association. On the basis of this statistically significant association, and given that that a strongly significant association also occurs between adherence and the *interventional fragility* indicator, it is surprising therefore that no significant association was to be found between either adherence or interventional fragility and cumulative pill intake or regimen complexity. The interventional fragility indicator was designed to predict whether patients will be able to adjust emotionally to the demands of physically and psychologically stressful medical protocols. Based on the assumption that increasingly complex regimens contribute to such emotional adjustment it is surprising that more associations were not found between adherence and measures of regimen complexity. For example, one could hypothesise that, given this assumption, and the association between self-reported adherence and the interventional fragility scale, one or other would be sensitive to higher dosing requirements, more antiretrovirals in combination, more pills in total, and a generally more complex treatment regimen. This did not prove to be the case in this research and may indicate that there are other mediating variables or factors, that are

not assessed by the measures used. Contextual and mediating factors may need further investigation concurrent with personality characteristics.

Despite such conclusions, the evidence yielded in this research would point towards self-report adherence as an essentially reliable measure. Other studies have also found this to be the case, and self-report remains the most cited measure of adherence in the literature on compliancy in life-threatening illnesses in general (Haubrich et al., 1999; Besch et al, 1997; Caron et al., 1985).

So far this discussion has identified that the demographic information yielded is largely anecdotal in its relevance to the adherence issue, although previous research has found statistical significance between adherence and such strata in surveys of large samples. The low sample size meant that this study was unlikely to detect any influences of demographic data even if they were present. The consideration of self-reported adherence as a potentially reliable measure of compliance has also been discussed using statistically significant findings, and further anecdotal observations, to support such a claim. Before continuing with a critique of those specific psychological elements that may or not have an influence on treatment adherence, it would be prudent to re-visit the research hypothesis as a reminder of the main objectives of this study:

Therapeutic and non-therapeutic levels of regimen adherence to HIV antiretroviral therapy are associated with:

i) personality style

ii) coping styles

iii) attitudes to, and beliefs about, healthcare for HIV illness

iv) treatment prognostic indicators

The specific components of this hypothesis will now be considered in turn and either endorsed or rejected based on an assessment of the evidence produced by the research.

4.2.1 Hypothesis i) - Therapeutic and non-therapeutic levels of regimen adherence to HIV antiretroviral therapy are associated with personality style

As the introduction to this area of research has demonstrated (*see section 1.3.4.2: Psychological variables and adherence to antiretroviral therapy)* explicit personality characteristics have been studied very little in the context of adherence to HIV treatment. Studies have tended to focus on aspects of mental health (for example, depression; Singh et al., 1994), cognitive barriers to treatment, self-efficacy and social support. Rhodewalt & Fairfield (1990) suggest that patients exhibiting the Type A behaviour pattern may be more likely to perceive medical regimens as threatening to their personal freedom and react with nonadherence in an attempt to regain perceived behavioural control. Christensen & Weibe (1996) in a review of the limited literature, report that chronically ill patients with an internal locus of control exhibit more favourable adherence. Most personality correlates of health-related outcomes have been studied in relation to other life-threatening conditions such as renal dialysis, and it is these investigations that must be consulted in respect of this research study.

The findings of this study indicate that the hypothesis can be upheld with regard to the relation between HIV treatment adherence and personality style. The results support that there is a statistical association between an *accommodating* personality style and adherence. Specifically, good adherers were more likely to possess this characteristic. There was also evidence for a statistical association between a *systematising* personality style and adherence. Good adherers were statistically more likely to have a systematising personality style.

An accommodating personality style describes an individual who,

"reacts to the passing scene, is accommodating to circumstances created by others, but at times can appear acquiescent". (MIPS technical manual)

A systematising personality describes individuals who,

"are highly organised, and predictable in their approach to life's experiences. They transform new knowledge in line with what is known and are careful, if not perfectionistic, in arranging even minor details. As a result, they are often viewed by others as orderly, conscientious, and efficient." (MIPS technical manual)

Upon a consideration of these synopses of each personality style, it becomes relatively effortless to begin associating such approaches to life to the context of an individual who consistently adheres to treatment regimens. Having such attention to detail and sense of order, routine and a willingness to adapt to the requests of others would undoubtedly be advantageous pre-requisites for a good ability to live with the demands imposed by combination therapy.

A conceptual examination of the five-factor taxonomy of personality dispositions (Costa & McCrae, 1992) suggests that conscientiousness may be the most accurate trait descriptor of those individual qualities important with regard to adherence behaviour. Digman (1990) and Costa & McCrae (1987) have described this personality dimension as reflecting

"a highly purposeful, well organised, self-disciplined style" or *"a will to achieve, dependability, and self-control".*

There would certainly appear to be a similarity between interpretations of the accommodating and systematising personality styles of this study, and those of the theorists above.

Christensen & Smith (1995) observed that conscientiousness was a five-factor trait significantly associated with adherence to medication regimens required during renal dialysis. No other personality dimension was found to be significantly associated with patient adherence.

This corroboration of support for the associative value of accommodating and systematising personality styles with HIV treatment regimens, leads to the conclusion that the hypothesis is endorsed in this respect. The findings of this study would appear to provide some support for a relationship between therapeutic levels of regimen adherence to HIV antiretroviral therapy and personality styles, coping styles and indicators of treatment prognosis.

4.2.2 Hypothesis ii) - Therapeutic and non-therapeutic levels of regimen adherence to HIV antiretroviral therapy are associated with coping style

The research base on coping styles and adherence to antiretroviral treatment is slightly wider than that of personality characteristics. Sherbourne et al. (1992) observed that avoidant coping behaviour has a negative association with medical treatment adherence. Active coping preferences have been found to predict better adherence outcomes in patients undergoing haemodialysis at home, where patient involvement and control is greater. Problem-focused coping strategies have also received some attention in the literature in relation to adherence. Folkman (1984) proposes that problem-focused coping strategies oriented toward modifying some aspect of the stressful situation may be associated with more positive outcomes only if the stressful situation is amenable to efforts to control it. Pugliese et al. (1995) studied adherence in cancer patients and discovered that a positive coping style was related to treatment compliance, although the term 'positive' coping style is rather a vague variable that requires elaboration.

Conversely, Wiebe & Christensen (1996) review how there is little evidence to suggest that the way an individual copes with a stressful encounter bears a predictable relationship to that individual's well-being. They note how previous research into coping may in part be due to a failure to consider contextual influences. There may be further evidence in this for a stronger consideration of the illness or treatment context as opposed to a single focus on the person in terms of the adaptational value of a particular style of coping.

Catz et al. (2000) also considered the role of barriers to treatment adherence in HAART. The findings in this study highlighted the need for interventions that help patients organise and manage their medication regimens, and help them to plan and problem-solve how they will handle regimens in the context of other life activities. The study did not, however, identify any coping styles related to medication adherence.

This research study found an association between *nonconforming* and *forceful* coping styles and medication adherence.

The nonconforming scale of the MBMD describes a coping style characterised by individuals who may be,

"……somewhat sceptical about the motives of others, and they tend to act insensitively and impulsively at time".

The MBMD also advises that,

"……such individuals should dealt with firmly and directly, with reassurance that healthcare professionals are there to help them solve their physical problems".

High scorers on the forceful scale are characterised as,

"tending to be rather domineering and tough-minded.....the healthcare team should try not to feel intimidated or provoked by these individuals. A straightforward approach is most effective with these patients.....they may not follow treatment regimens well.....extra effort will be necessary to encourage them to comply".

As with the descriptions of those personality styles found to be significantly associated with adherence, it is not difficult to map individuals with difficulties adhering to treatment within these contexts. Therefore it is concluded that the hypothesis is also endorsed with respect to its prediction that treatment adherence would be significantly associated with coping style.

4.2.3 Hypothesis iii) - Therapeutic and non-therapeutic levels of regimen adherence to HIV antiretroviral therapy are associated with attitudes to, and beliefs about, healthcare for HIV infection

The review of the literature uncovered that there was a research base in how negative attitudes about healthcare and illness may also interfere with treatment adherence. For example, Youssef (1984) reports on reasons cited by the mentally ill for not taking medications, such as a fear of addiction, or a belief that medication use was a sign of weakness. Among HIV-infected individuals, attitudes and beliefs related to decreased adherence have been found to include the patient's perception and acceptance of the disease, and a perceived lack of benefit (Norris et al., 1990). A denial of the necessity of treatment has also been found to impede adherence.

The Gordillo et al. (1999) study evaluated patients' belief in antiretroviral therapy, knowledge about the illness and satisfaction with their clinician. Although these variables were well reported within their sample, none were found to be associated with compliance.

This research study used two scales of the MBMD to measure patient attitudes and beliefs by proxy. These scales lay within the Stress Moderators domain of the MBMD and consisted of *illness apprehension* versus *illness acceptance* and *future pessimism* versus *future optimism*. Neither scale measured any significant associations with adherence, and consequently, the relevant component of the hypothesis was rejected.

4.2.4 Hypothesis iv) - Therapeutic and non-therapeutic levels of regimen adherence to HIV antiretroviral therapy are associated with treatment prognostic indicators

The use of indicators that could potentially inform the prognosis of a course of illness in terms of treatment adherence would appear to be very rare. A literature review revealed no specific working measure for determining patient adherence. Perhaps this should be obvious, as if there were such a reliable instrument available, there would be much less of a research base on adherence in chronic illnesses such as HIV. For the purposes of this research, a Treatment Prognostics Domain within the MBMD, was used to evaluate if any statistical association existed between adherence by self-report and a range of scales designed to measure such treatment adherence issues such as: interventional fragility, medication abuse, information discomfort, excessive utilisation of services, and problematic compliance. To this extent, such an evaluation was seen as particularly novel, especially as the MBMD was a new assessment instrument despite being developed from the Millon Behavioural Health Inventory (MBHI).

Two scales were found to be significantly associated with treatment adherence: *interventional fragility* and *problematic compliance.*

The MBMD estimates that approximately 25-30% of all medical patients have compliance problems. The scale describes individuals who,

"……are disinclined to follow homecare advice on treatment, and to keep and be on time for appointments"

The results indicated that good adherers are statistically less likely to have the problematic compliance characteristic. This was potentially a very interesting result as it could have implications for the credence of applying the MBMD as a screening tool in HIV healthcare settings. The significant associations noted between adherence and other scales on the assessment would certainly further support this notion. Therefore it is felt that future research could concern itself with applying the MBMD to a much larger HIV-infected sample, with the objective of avoiding the limitations experienced with a sample size as low as the 25 participants assessed in this current research.

The finding that *interventional fragility* was statistically associated with adherence would give further strong evidence to suggest that the treatment prognostics indicators of the MBMD are potentially very reliable in identifying those HIV-infected individuals likely to be experiencing adherence difficulties, not only currently, but also at some point in the future.

These findings enabled the hypothesis to be supported regarding its prediction of the association of treatment prognostics indicators with treatment adherence.

4.3 Limitations of the study and implications for clinical practice and future research

Despite the significant statistical associations revealed by this study, it is still believed that the extent of analysis and the exploration of inferential statistics was impeded by the low sample size. In order to achieve statistical power = 0.8 (alpha = 0.05) and a medium effect size, a sample size of N = 67 was required. This would undoubtedly have enabled more powerful multivariate analyses to be carried out. However, the fact that statistical significance was achieved, and that self-reported adherence was arguably a particularly reliable method of evaluating treatment adherence, would all suggest that the measures used were especially sensitive at tapping into the psychological factors considered.

Interpretation of the extent of statistical significance should also perhaps be approached with caution. Level of probability for statistical significance was set at $p<0.05$ in the analysis; this may have had an amplification effect on the frequency of statistically significant results due to the multiple comparisons being made in the chi- square analysis. It could be argued that the data should be analysed further with some adjustment for p value taken as level of statistical significance. To summarise the limitations of this research, the author concludes that interpretation of results should be tempered by the small sample size, the low take-up during recruitment of participants, the considerable number of comparisons made during the analysis, and the implied potential for an undermined representation of the sample population.

Recruiting participants for a study such as this can become problematic when the research population is an outpatient group, and contact between the researcher and participants is determined by outpatient appointment times. Many of the potential participants travelled considerable distances to attend the Lothian-based Regional Infectious Diseases Unit, and with appointment frequency often as low as only once every three months, the efficient distribution of information about the study was a

cumbersome yet crucial task. It is also important to be aware that biases may also have existed in the sample investigated. The researcher was aware that those individuals who agreed to take part, may have represented a particularly motivated subgroup of the sample. Working on the assumption that the more motivated individuals were most likely to exhibit positive adherence behaviours, the potential therefore existed of failing to obtain a truly representative sample in terms of treatment adherence.

It is also noteworthy that there is still unfortunately some stigma attached to HIV/AIDS, and this may have led to patients approaching the research with some ambivalence.

Critics of the self-report method of collecting data may argue that there are inherent problems in obtaining accurate and reliable responses from patients regarding what can often be a contentious issue of treatment adherence. This argument may be more applicable to the use of structured self-report questionnaires. However, the use of an informal semi-structured interview to facilitate self-report was certainly believed to enhance the accurate reporting of adherence variables among this HIV positive population. Collection of accurate adherence data may also have been enhanced by the fact that each respondent was being interviewed by someone they were unfamiliar with, and with whom they could perhaps be more open and honest with in their responses.

This research also suggested some evidence for the role of mediating factors in the association between adherence, personality characteristics and coping styles.

Potential for future research may include the comparison of the application of similar measures across individuals with other life-threatening illnesses requiring optimum levels of treatment adherence.

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Appendix I

Summary of process of obtaining ethical approval

The process of application for ethical approval to undertake the research study is summarised in the following steps. Please refer to the relevant correspondence as indicated within the summary.

Step 1: An application form (appendix 1a) was forwarded to the Lothian Research Ethics Committee on 5 February 2002. Attached to the application was a full protocol (appendix 1b) detailing the research objectives and methodology, a copy of the research participant consent form (appendix 1c), a research participant information sheet (appendix 1d), a consultant information sheet (appendix1e). Finally, copies of each questionnaire to be used in the research were also included (refer to appendices 2, 3 &5).

Step 2: Simultaneously, verbal and written consent was obtained from each Lead Consultant at the Regional Infectious Diseases Unit, Western general Hospital and the Department of Genito-Urinary Medicine, Edinburgh Royal Infirmary (refer to appendix 1f) for related correspondence.

Step 3: The application and research protocol were considered for ethical approval by The Psychiatry/Clinical Psychology Research Ethics Sub-Committee at a meeting held on 20 February 2002. Simultaneously, the application underwent a review of resource and financial implications, which was subsequently approved by the Research and Development Office, Royal Infirmary of Edinburgh. (Refer to correspondence, appendix 1g)

Step 4: On 26 February 2002 the Research Ethics Sub-Committee agreed to grant ethical approval subject to the amendments stated in their correspondence (appendix 1h).

These amendments were then also forwarded.

Step 5: At a meeting of the Research Ethics Sub-Committee held on 20 March 2002 ethical approval was granted to proceed with the research study. The researcher received an official Certificate of Ethical Review on 12 April 2002 (appendix 1i). The research protocol was then activated.

Appendix Ia

Lothian Research Ethics Committee
Application form and notification of receipt

LOTHIAN RESEARCH ETHICS COMMITTEE
APPLICATION FORM

For official LREC Use Only	*For official LREC Use Only*
LREC/ / /	

INSTRUCTIONS: Please complete in type. Please place a circle around Yes/No options as appropriate. A version of this form is available on disc from the Secretary of the LREC or from your Trust R&D Office. ONE COMPLETE COPY OF YOUR APPLICATION FORM AND PROTOCOL SHOULD BE SENT TO YOUR R&D OFFICE.

It is essential that this form is completed fully and sent with relevant enclosures. **You should not simply refer to the protocol but complete the form with the information requested.** Please refer to the accompanying Guidance Notes when completing the form and complete the checklist before sending. Where a question is not applicable it is important to make this clear and not to leave it blank. **It is important that the language used in this application is clear and understandable to lay members.** All abbreviations should be explained.

Applicant's Checklist

Please indicate if the following have been enclosed by underlining or placing a circle round Yes/No/Not applicable options.

Application Form (**seventeen** copies)	Yes	No	
Full protocol (**seventeen** copies)	Yes	No	Not applicable
Application Fee of **£500**	Yes	No	~~Not applicable~~
Research subject consent form (**seventeen** copies)	Yes	No	Not applicable
Research subject information sheet (**seventeen** copies)	Yes	No	Not applicable
Advertisement for research subjects (**seventeen** copies)	Yes	No	~~Not applicable~~
GP/consultant information sheet or letter (**seventeen** copies)	Yes	No	Not applicable
Interview schedules for research subjects (**seventeen** copies)	Yes	No	Not applicable
Letters of invitation to research subjects (**seventeen** copies)	Yes	No	Not applicable
Questionnaire* ~~Finalised~~/Not yet finalised (**seventeen** copies)	Yes	No	Not applicable
Researchers brochure or data sheet for all drugs (**one** copy only)	Yes	No	~~Not applicable~~
Statement on compensation arrangements (**seventeen** copies)	Yes	No	~~Not applicable~~
CTX/CTC/DDX (**one** copy only)	Yes	No	~~Not applicable~~
Annexe A** (**seventeen** copies)	Yes	No	~~Not applicable~~
Annexe B*** (**seventeen** copies)	Yes	No	~~Not applicable~~
Annexe C**** (**seventeen** copies)	Yes	No	Not applicable

* *Please indicate whether or not this is the final version*

** *Required if the study involves the use of a new medicinal product or medical device, or the use of an existing product outside the terms of its product licence. Annexe A is attached to the Application Form.*

*** *Required if the study includes the diagnostic use of ionising, radiation (radioactive materials or X-Rays). Annexe B is attached to the Application Form.*

***** Information concerning local researchers should always be given where possible at this stage. Annexe C is attached to the Application Form. Please make additional copies as necessary.*

SECTION 1 — Details of applicant(s)

1. Short title of project:
The role of personality factors in adherence to drug treatments for HIV

Full title:
An investigation into how normal and abnormal personality characteristics correlate with level of adherence to antiretroviral therapy in individuals with HIV infection

2. Principal researcher (responsible for dealing with the LREC and the local R&D Office who will be the sole point of contact and through whom all correspondence will be channelled)

Surname:

Ferguson

Forename:

John

Title:

Mr

Present appointment of applicant:

Psychologist in Clinical Training

Qualifications:

Bsc Combined Honours (Psychology & Biology)

Address:

Studio Flat, 10 Boswall Road, Trinity, Edinburgh, EH5 3RH

Tel:

Mobile: **07796 – 351827**
Work: **0131 – 537 8300**

E-Mail:

J.S.Ferguson-3@sms.ed.ac.uk

3 Please give an approximate figure for the number of trials/studies in which the principal researcher has been involved over the past year

One small-scale research project on a child psychology training placement

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4. Names, titles and qualifications of other local researchers working on this project

N/A

---

5. Who is sponsoring the study?

Contact name:

Ms Ann Green (Line Manager)

Organisation:

East of Scotland Training Course in Clinical Psychology

Address:

C/o Nicole Tait
Secretary to Ann Green
Level 4
Kennedy Tower
Royal Edinburgh Hospital
Morningside Park
Edinburgh EH10 5DF

Tel:

0131 - 5376280

E-Mail:

N/A

---

6. Drug Company Reference Number

N/A

---

7. Funding

Please give full details where applicable of:

a) Payment to subjects

N/A

b) Payment to Trust/practice/research funds, etc. *(specify institution(s))*

N/A

c) Personal payment or personal benefit to researcher

N/A

Is payment:

i)	A block grant	*Yes*	*No*
ii)	Based on the number of research subjects recruited?	*Yes*	*No*
	If yes, how much per patient:		

d) Details of other benefits, e.g. equipment

N/A

e) Details of NHS Trusts and hospitals/facilities to be used

Regional Infectious Diseases Unit, Western General Hospital, Edinburgh

f)	**Will the costs incurred by the institution be covered by the payment?**	*Yes*	*No*

---

8. What other researchers are/do you intend to be involved in this project? (Details of researchers added subsequently must be notified to the LREC)
Please use the form attached at Annexe C

N/A

SECTION 2 — Details of project

*This section must be completed fully. A copy of the protocol should be enclosed with the application form, but it is **not** sufficient to complete questions by referring to the protocol.*

9. Aims and objectives of project *(Maximum. 250 words)*

To attempt to identify correlates between normal/abnormal personality factors and level of adherence to combination therapy in individuals with HIV positive status.

Sherr (2000), in a review of the literature on adherence in HIV treatment, concludes that adherence can be studied from four main perspectives:

- The patient or person
- The preparation/medication
- The provider
- The place or setting

She then describes how a number of psychological theories can be invoked to understand non-adherence in terms of these four levels: Cognitive models, Psychodynamic models, Social concepts and Personality concepts. This project aims to develop this principle further by studying how personality *specifically* may influence a person's adherence to treatment regimens in HIV.

A review of the literature reveals an enormous amount of studies of adherence to HIV treatment. However, very few of these studies explicitly examine the role of personality in adherence. The concept underpinning the study is to investigate if it may be possible to predict likely adherence to HIV combination therapy based on the presence (or absence) of certain personality characteristics. The end-point to this research is to begin debating methods of improving adherence to antiretroviral therapy at an individual level.

Sherr, L. Understanding adherence. Leading Article in Journal of HIV Therapy, 2000, Vol. 5 No. 2 pp 30-35

10. Scientific background of study *(Maximum. 250 words)*

Studies on factors which influence adherence to HIV therapies are widespread. With HIV treatment, a high level of adherence is vital if viral suppression is to be sustained. It is clear that non-adherence is very common among patients treated for HIV infection. By understanding adherence factors in HIV, interventions can be generated and evaluated to increase treatment adherence. Personality theory would examine individual attributes in order to explain adherence. From the personal perspective, an explanation would be related to ideas such as self-efficacy, self-esteem, resilience, commitment and motivation. Personality variables may also affect the extent to which the physician can present persuasive information and explanatory data thus influencing a variety of client-doctor relationships.

The role of personality factors in adherence to HIV treatment is not well documented in the literature. There appears to be a paucity of research in this area. Personality variables and treatment adherence have been more frequently researched in relation to other life-threatening conditions such as diabetes and cancer. Results of these studies have identified personality variables characteristic of 'good' and 'poor' adherers to treatment.

Using a well documented and contemporary biopsychosocial theory of personality developed by Theodore Millon (Davis 1999), this study will examine the personality styles of the participants and attempt to identify correlations between certain personality variables and level of adherence to HIV treatment. The personality assessments proposed to be used in the study have been developed as a result of Millon's dimensional conceptualisation of personality.

Davis R. D. (1999). Millon: Essentials of his science, theory, classification, assessment and therapy. Journal of Personality Assessment, 72(3): pp330-352

11. Brief outline of project including outcome measures *(Maximum. 250 words)*

To achieve statistical power around 70 participants will need to be recruited for this project. Individuals attending the Infectious Diseases Unit, Western General Hospital and the GUM clinic at Edinburgh Royal Infirmary will be approached with information about the study. Subject to their consent to take part, each participant will meet with the researcher and be invited to complete a small battery of questionnaires in 'pencil & paper' format. The battery of assessments will consist of:

- A short demographic questionnaire
- A brief self-report questionnaire on treatment adherence
- A questionnaire evaluating perceived quality of therapeutic relationship with consultant
- The Hospital Anxiety and Depression Scale (HADS)
- The Millon Index of Personality Styles (MIPS)
- The Millon Clinical Multiaxial Inventory –Third Version (MCMI-III)

It is estimated that the entire assessment battery will take 1hr – 1hr 15mins. to complete. The researcher will be present during completion of the assessment.

The MIPS is designed for use by professionals looking for a comprehensive, well-rounded report of general personality. It is a standardised psychological assessment containing 180 unobtrusive True/False items organised into 3 groups of scales, together with 3 validity indicators or response sets: Motivating Aims, Interpersonal Behaviours, Cognitive Modes, Response Sets.

The MCMI-III is a standardised instrument which assesses abnormal personality characteristics. It specifically evaluates emotional, behavioural and interpersonal difficulties and can help to assess DSM-IV related personality disorders and clinical syndromes. It consists of 175 True/False items grouped into 14 personality pattern scales and 10 clinical syndrome scales.

Both tests draw from Dr T. Millon's widely accepted theory of personality.

Concurrent with personality assessment the researcher will also consult a computerised database of patient information located at the Infectious Diseases Unit, Western General Hospital. This database will reveal the level of adherence of each patient according to frequency of inpatient visits and viral load over time (a physiological marker of adherence to treatment).

Correlations between personality variables and level of treatment adherence will be examined upon statistical analysis of the data. Multiple regression will be used for statistical analysis.

12. Proposed start date and duration of project

Recruitment of participants data collection is proposed to take place during March, April and May 2002. Recruitment will commence immediately following ethical approval. Data Analysis and report formulation will be on-going through June and July with a complete final report submitted by the end of August 2002.

13. Study design (e.g. Randomised Controlled Trial, cohort, case control, epidemiological analysis)

The study will, to some degree, constitute an epidemiological analysis of personality characteristics common amongst the research sample. The study will be cross sectional in design. Concurrent with a structured personality assessment, the researcher will also record a physiological measure of adherence (from a computerised database of viral load over time). Correlations between personality variables and level of treatment adherence will be examined upon statistical analysis of the data. Multiple regression analysis will be used to examine the extent to which levels of regimen adherence is predictable from variations in demographics, anxiety, depression, perceived quality of therapeutic relationship with consultant, and a range of personality characteristics and clinical personality pathology. A between groups design will examine the differences in variation of these variables across three levels of treatment adherence.

---

14. Size of the study (including controls)

Will the study involve:

(a) Human Subjects *Yes* *No*

i) How many patients will be recruited?

Preliminary research suggests that this study will require around 70 participants in order to achieve statistical power. See power analysis below.

ii) How many controls will be recruited?

N/A

iii) What is the primary end point?

The recruitment of at least 70 participants

iv) How was the size of the study determined?

Examination of previous similar studies on adherence and personality factors cited in a review of the literature in this area. These studies concerned other life-threatening conditions where adherence was an important factor.

v) What is the statistical power of the study?

For Power = 0.8 (alpha = 0.05) and a medium effect size, N = 67 for 2 independent variables. (Cohen, 1992)

(b) Patient Records *Yes* *No*

i) How many records will be examined?

At least 70, ie. the case notes/computer database information of each participant will be reviewed.

ii) How many control records will be examined?

N/A

iii) What is the primary end point?

See above

iv) How was the size of the study determined?

See above

v) What is the statistical power of the study?

See above

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15. Scientific critique

Has the protocol been subject to scientific critique? If so, please give the following information:

If the critique formed part of the process of obtaining funding, please give the name and address of the funding organisation:

N/A

If the critique took place as part of an internal process, please give brief details:

The scientific critique of this protocol has taken place in collaboration with Dr Suzanne O'Rourke (Research Academic Supervisor) and Dr Alison Richardson (Research Field Supervisor). The protocol is entirely evidenced-based and was developed by consulting the most contentious literature available. The psychological and theoretical framework behind this study is fully explained within the research protocol attached.

If no critique has taken place, please explain why, and offer justification for this:

N/A

If you are in possession of any referees' or other scientific critique reports relevant to your proposed research, please forward copies with your application form.

SECTION 3 — Recruitment of subjects

16. Local Recruitment of Subjects

a) How many subjects are being studied within Lothian?

70

b) Are any of these subjects involved in existing research or have been involved in any recent research in the last six months? (Yes) *No*

If yes, please justify their use in this project

Some participants have been involved in drugs trials in the past. Their use in this project is justified because the study is strongly linked to their experience of taking drugs.

c) Will any of the subjects involved be in a dependent relationship with the researcher? *Yes* (No)

If yes, please ensure you comply with local recruitment arrangements

d) Local independent adviser details:

Mike Henderson, Senior Clinical Tutor, Doctorate of Clinical Psychology, Kennedy Tower, Royal Edinburgh Hospital

I confirm that I am willing to act as an Independent Adviser.

Signature of Independent Adviser: Richard Hall

Date: 1/3/2

e) Will any of the subjects involved be medical students? *Yes* (No)

If yes, please obtain signed agreement of the Dean of the Faculty of Medicine:

Signature the of Dean of the Faculty of Medicine
or equivalent if medical students are research subjects: .....

17. How will the subjects in the study be:

a) selected?

Participants will have an HIV positive status. They will be currently receiving antiretroviral medication and will have been in attendance at the Regional Infectious Diseases Unit, Western General Hospital during at least the preceeding six months.

b) recruited?

A letter will be sent to each consultant physician at the Unit to request their consent to approach his or her patients with regard to taking part in the study. Each consultant will also be sent an information sheet explaining the study's objectives and methodology. Pending consent from each consultant, potential participants will be approached with information and a letter inviting them to consider taking part in the study. They will have at least 24 hours to consider this. Willing participants will then be sent an appointment to meet with the researcher to obtain formal written consent and complete questionnaires.

Patients will also be approached with information on the wards following consent from their consultant. This will involve the distribution of information amongst nursing staff on wards. The researcher will also be in attendance at the Unit should any patients wish to approach him about the research.

c) what inclusion criteria will be used?

Participants must currently be in receipt of antiretroviral medication and have been in attendance at the Unit within at least the previous six months.

d) what exclusion criteria will be used?

Those patients under the influence of illegal drugs during psychological testing will be excluded from the study.

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18. How will the control subjects group (if used) be: *(Type N/A if no controls)*

a) selected?

N/A

N/A

b) recruited?

N/A

N/A

c) what inclusion criteria will be used?

d) what exclusion criteria will be used?

SECTION 4 — Consent

19. Is *written* consent to be obtained? (Yes) No

If yes, please attach a copy of the consent form to be used. Enclosed

If no written consent is to be obtained, please justify.

Patients will have at least 24 hours time in which to consider whether or not to consent.

20. How long will the subject have to decide whether to take part in the study?

If less than 24 hours please justify.

N/A

21. Please attach a copy of the written information sheet or letter to be given to the subject.

(See Guidelines page 3 and Appendix A.) Enclosed

If no Information Sheet is to be given, please justify.

N/A

22. Have any special arrangements been made for subjects for whom English is not a first language? *Yes* *No* (N/A)

If yes, give details.

If no, please justify.

23. Will any of the subjects or controls be from one of the following vulnerable groups?

Children under 16

People with learning difficulties

Unconscious or severely ill

Other vulnerable groups e.g. mental illness, dementia

(Yes) No

If yes, please specify and justify:

Participants will have an HIV positive status and may possibly be facing a life-threatening illness. Justification resides in the research outcome of debating methods of improving treatment adherence.

24. What special arrangements have been made to deal with the issues of consent for the subjects above? *(Please see Guidelines.)*

Patients unable to give informed consent will be excluded from the study.

SECTION 5 Details of interventions

25. Does the study involve the use of a new medicinal product or medical device, or the use of an existing product outside the terms of its product licence? *(Please see Guidelines.)* *Yes* (No)

If yes, please complete Annexe A of the Application Form.

26. Will any additional diagnostic tests using ionising radiation (radioactive materials or X-Rays be administered? *Yes* (No)

(NB Please ensure information in Question 17 includes exclusion criteria with regard to ionising radiation if appropriate.)

If yes, please complete Annexe B of the Application Form.

27. Please list those procedures in the study to which subjects will be exposed indicating those which will be part of normal care and those that will be additional (e.g. taking more samples than would otherwise be necessary). Please also indicate where treatment is withheld as a result of taking part in the project.

Participants will be required to complete two structured paper and pencil personality assessments each lasting 25-30 minutes. They will also be asked to complete a short demographic questionnaire, a short screening questionnaire for anxiety and depression symptoms, and brief questionnaires relating to their own self-report of medication adherence and their perception of the quality of the therapeutic relationship with their consultant. The above procedures are in addition to normal care. The study does not involve the with-holding of any treatment.

SECTION 6 Risks and ethical problems

28. Are there any potential hazards? *Yes* (No)

If yes, please give details, and give the likelihood and details of precautions taken to meet them, and arrangements to deal with adverse events.

29. Is this study likely to cause any discomfort or distress? *Yes* (No)

NOT LIKELY.

If yes, please give details and justify.

It is possible, but very unlikely, that some participants may experience some discomfort in answering items about themselves within the personality questionnaires. The researcher will be present during completion of these questionnaires to talk through any possible discomfort with the participant should it become apparent.

30. Safety Requirements

a) Medical support and other facilities available:

N/A

b) Local emergency contact details:

N/A

c) If you are going to administer drugs what arrangements have you made to store, code and administer them? *(See Annexe A)*

N/A

I confirm that I am aware of and approve of these arrangements.

Signature of Hospital Pharmaceutical Officer: .....

Date: .....

d) Are you going to administer radioactive materials? *Yes* (No)
(See Annexe B)

i) If yes, do you have a separate ARSAC certificate for this particular research study? *Yes* *No*

ii) Have you informed the Radiation Protection Adviser? *Yes* *No*

I confirm that I am aware of and approve of these arrangements.

Signature of Radiation Protection Adviser: .....

Date: .....

31. What particular ethical problems or considerations do you consider to be important or difficult with the proposed study?

Please give details.

N/A

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32. Will information be given to the patient's General Practitioner? *Yes* (*No*)

Please note: permission should always be sought from research subjects before doing this.

If yes, please enclose an information sheet/letter for the GP.

If no, please justify:

Justified on the grounds that permission will be sought from the responsible medical consultant.

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33. If the study is on hospital patients, will permission of all consultants whose patients are involved in this research be sought? (*Yes*) *No*

If no, please justify:

---

34. Are you free to publish the results of this study?

(*Yes*) *No*

If no, please expand:

X

SECTION 7 Compensation and confidentiality

Product liability and consumer protection legislation make the supplier and producer (manufacturer) or any person changing the nature of a substance, e.g. by dilution, strictly liable for any harm resulting from a consumer's (subject or patient) use of a licensed product.

35. Have arrangements been made to provide indemnity and/or compensation in the event of a claim by, or on behalf of, a subject for non negligent harm?
(Please indicate N/A if not applicable)

Yes *No* (*N/A*)

If yes, please give details of compensation arrangements with this application.

For pharmaceutical company sponsored research, the company should confirm that it will abide by the most recent ABPI guidelines *(Manual V.14.1.1)*

36. In cases of equipment or medical devices, have appropriate arrangements been made with the manufacturer to provide indemnity?

(Please indicate N/A if not applicable) *Yes* *No* (*N/A*)

If yes, please give details and enclose a copy of the relevant correspondence with this application.

37. Will the study include the use of any of the following?

Audio/video recording *Yes* (*No*)

Observation of patients *Yes* (*No*)

If yes to either:

i) How are confidentiality and anonymity to be ensured?

ii) What arrangements have been made to obtain consent for these procedures?

38. Will medical records be examined by research worker(s) outside the employment of the NHS? *Yes* (*No*)

If yes, please see Guidelines.

39. What steps will be taken to safeguard confidentiality of personal records?

All information provided by participants will be treated in the strictest confidence. Medical records (either hard copy or computer database held) will be viewed by the researcher only. Information leaving the Unit will have all identifiers removed. Participant consent forms will be kept separately from completed questionnaires and individual participant numbers will be allocated to ensure anonymity. Participants could not and would not be identified in any subsequent report or publication.

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40. What steps will be taken to safeguard the information relating to specimens and the specimens themselves?

N/A

SECTION 8 — Management Details

41. Can this project be included in the NRR (National Research Register) **?** *Yes* (No)

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42. Is this research carried out as part of a: **Undergraduate Degree?** *Yes* (No)

Student Special Study Module? *Yes* (No)

Postgraduate Degree? (Yes) *No*

If **YES** which one?
Doctorate of Clinical Psychology – University of Edinburgh

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43. Is the host Trust the Lead Institution for this project? *Yes* (No)

If **No,** please indicate Lead Institute
Doctorate of Clinical Psychology – University of Edinburgh

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44. Please specify the amount of funding requested/received from the funding body.
N/A

Funding Body	Funding Amount	Duration of Funding	Expected Date for Outcome of Grant Application	Funder's Ref. No.

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45. Please indicate all specialties involved in this project (including contact person):

Biochemistry		Medical Physics/ Engineering	
Biomedical Engineering		Medical Statistics	
Community Services		Microbiology	
Cytogenetics		Midwifery Services	
Dental Technology		Nuclear Medicine	
Dieticians		Nursing	
ECG		Occupational Therapy	
GP		Pathology	
Haematology		Pharmacy	
Health Education/Promotion		Physiotherapy	
Imaging/Radiology		Psychology	
Immunology		Speech Therapy	
Information Technology		Virology	
Medical Illustration/ Photography		Other	

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46. Who has vetted the contract?

- [ ] Commercial Development Unit (CDU)
- [ ] University (Edinburgh Research and Innovation)
- [ ] Trust

☐ Not Applicable

SECTION 9 NHS Resource Implications/Costs

47. Time Resources N/A

a) Staff involved in execution of project (including principle researcher)

Name	Grade of Staff	Hours on project (specify per week or per patient or overall) Please estimate as accurately as possible, you should include hours outside your contracted hours	Funded by: Please state the funder of the research time. (e.g. Trust/Univ/funds specific to this project/ other sources)
1.			
2.			
3.			
4.			
5.			
6.			
7.			
8.			

b) Additional time (Please estimate time spent on grant application/Ethics submissions/ Protocol development etc, before project start)

Category	Details	Estimated Total hours
Associated Grant Applications		
Ethics submissions		
Protocol development		
Other		

48. a) Could this activity be carried out within the Wellcome Trust Clinical Research Facility (WT-CRF), with centralised research nursing, tracking and administration?

Yes *No*

b) If yes, are you intending to apply to the WT-CRF Scientific Committee?
(If yes, contact the WT-CRF office on 0131 537 2591)

Yes *No*

49. Service Costs

a) Is your study likely to incur excess treatment/ investigation costs? *Yes* *No*

b) Additional Service Costs (including contact person)

Location of research	Quantity per patient	Contact Person
Additional Ward Days		
Additional Outpatient Visits		
Additional hours/procedures in Theatre		
Additional GP time		
Other – please give details		

50. **What additional Investigations are involved per patient?** (Please discuss the NHS resources needed with the relevant departments and obtain their agreement)

NOTE FOR SIGNATORIES

IF YOU ARE UNSURE AS TO WHETHER THIS WILL BE ACCEPTABLE TO YOUR PATIENT SERVICES DIRECTOR/HEAD OF DEPARTMENT, THEN PLEASE DISCUSS WITH THEM BEFORE SIGNING.

(a) Nursing			
Grade of staff & Hours involved			
Description of activities involved			
Additional no. of contracts			
Funded from:	This grant	**Yes**	**No**
	Department	**Yes**	**No**
	Commercial/other sources	**Yes**	**No**

Agreed by Directorate Clinical/Operational Manager (see list of authorised Trust signatories):

Signature: ..... Designation:.....Date: .....

(b) Pharmaceutical Implications			
Drugs involved			
Grade of staff & Hours involved			
Additional cost of drug therapy			
Additional dispensing requirements and storage & costs			
Funded from:	This grant	**Yes**	**No**
	Department	**Yes**	**No**
	Commercial/other sources	**Yes**	**No**

Agreed by Chief Pharmacist/Departmental Pharmacist (see list of authorised Trust signatories):

Signature: ..... Designation:.....Date: .....

(c) PROFESSIONS ALLIED TO MEDICINE (PAMS e.g. Occupational Therapists, Speech Therapists, Physiotherapists, Dieticians, Chiropodists)			
Grade of staff & Hours involved			
Description of activities involved			
Additional no. of contracts			
Funded from:	This grant	**Yes**	**No**
	Department	**Yes**	**No**
	Commercial/other sources	**Yes**	**No**

Agreed by Divisional Therapy Services Co-ordinator (see list of authorised Trust signatories):

Signature: ..... Designation:.....Date: .....

(d) Anaesthetics/Theatres/ITU/HDU/Day Surgery			
Description of activities involved			
Grade of staff & hours involved			
Funded from:	This grant	**Yes**	**No**
	Department	**Yes**	**No**
	Commercial/other sources	**Yes**	**No**

Agreed by site-based Operational Manager (see list of authorised Trust signatories):

Signature: ..... Designation:.....Date: .....

(e) Cardiac Laboratory Testing (e.g. ECG/Exercise Testing/Lung Function Test)			
Name of Test			
Number per patient			
Grade of staff & hours involved			
Funded from:	This grant	**Yes**	**No**
	Department	**Yes**	**No**
	Commercial/other sources	**Yes**	**No**

Agreed by site Chief Technician (see list of authorised Trust signatories):

Signature: ..... Designation:.....Date: .....

(f) Radiology/Imaging Procedures			
Description of activities involved			
Grade of staff & Hours involved			
Number per patient			
Funded from:	This grant	**Yes**	**No**
	Department	**Yes**	**No**
	Commercial/other sources	**Yes**	**No**

Agreed by site-based R&D Consultant for Radiology (see list of authorised Trust signatories):

Signature: ..... Date: ..... Rev'd by Radiology Ops Mgr:..... (Initials)

(g) A&E/ Acute Receiving Unit/ Medical Assessment Unit/ MOPD			
Description of activities involved			
Grade of staff & Hours involved			
Number per patient			
Funded from:	This grant	**Yes**	**No**
	Department	**Yes**	**No**
	Commercial/other sources	**Yes**	**No**

Agreed by site-based Operational Manager (see list of authorised Trust signatories):

Signature: ..... Designation: ..... Date: .....

(h) Haematology Laboratory Investigations			
Name of Test			
Grade of staff & hours involved			
Number per patient			
Funded from:	This grant	**Yes**	**No**
	Department	**Yes**	**No**
	Commercial/other sources	**Yes**	**No**

Agreed by Head of Site Laboratory (see list of authorised Trust signatories):

Signature: ..... Date: ..... Rev'd by Haematology Ops Mgr:..... (Initials)

(i) Clinical Biochemistry Laboratory Investigations			
Name of Test			
Grade of staff & hours involved			
Number per patient			
Funded from:	This grant	**Yes**	**No**
	Department	**Yes**	**No**
	Commercial/other sources	**Yes**	**No**

Agreed by Head of Site Laboratory (see list of authorised Trust signatories):

Signature: ..... Date: ..... Rev'd by Biochemistry Ops Mgr:..... (Initials)

(j) Pathology Laboratory Investigations			
Name of Test			
Grade of staff & hours involved			
Number per patient			
Funded from:	This grant	**Yes**	**No**
	Department	**Yes**	**No**
	Commercial/other sources	**Yes**	**No**

Agreed by Head of Site Laboratory (see list of authorised Trust signatories):

Signature: ..... Date: ..... Rev'd by Pathology Ops Mgr:..... (Initials)

(k) Other Laboratory Investigations (e.g. Med. Microbiology/Medical Physics/ Cytogenetics/Molecular Genetics/Medical Photography)			
Name of laboratory			
Name of Test			
Grade of staff & hours involved			
Number per patient			
Funded from:	This grant	**Yes**	**No**
	Department	**Yes**	**No**
	Commercial/other sources	**Yes**	**No**

Agreed by Head of Site Laboratory (see list of authorised Trust signatories):

Signature: ..... Date: ..... Rev'd by relevant Ops Mgr:..... (Initials)

(l) High Cost Consumables (e.g. Hickman lines, platinum coils etc.)			
Name of consumable			
Name of Test			
Number per patient			
Cost of Each			
Funded from:	This grant	**Yes**	**No**
	Department	**Yes**	**No**
	Commercial/other sources	**Yes**	**No**

Agreed by Directorate Operational Manager (see list of authorised Trust signatories):

Signature: ..... Designation:.....Date: .....

(m) Additional equipment purchased specifically for study			
Type of equipment			
Cost of equipment			
Funded from:	This grant	**Yes**	**No**
	Department	**Yes**	**No**
	Commercial/other sources	**Yes**	**No**

Agreed by Directorate Operational Manager (see list of authorised Trust signatories):

Signature: ..... Designation:.....Date: .....

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51. What additional Trust Administration support is involved? N/A

Secretarial/clerical (Grade of Staff)	**Hours per week on R&D**
Medical Records **Please state the number of case notes to be retrieved**	At least 70
Who will retrieve the Medical Records? (Medical records staff/researcher/student etc)	The Researcher

---

PLEASE ENSURE THAT YOU COMPLETE THE CHECKLIST ON THE FRONT COVER OF THE APPLICATION FORM AND ENCLOSE ALL RELEVANT ADDITIONAL DOCUMENTS.

SECTION 10	Declaration

DECLARATION

The information in this form is accurate to the best of my knowledge and belief and I take full responsibility for it.

I understand it is my responsibility to obtain management approval where appropriate from the relevant NHS body before the project takes place.

I agree to supply interim and final reports on the pro forma provided, and to advise my sponsor, the LREC from which approval was granted for this proposal and any other researchers taking part in the project of any adverse/or unexpected events that may occur during this project.

Signature of Principal Researcher:

Date:.....05.02.02.....

Annexe C	Local Researchers

OTHER RESEARCHERS INVOLVED IN THIS STUDY

Please provide the name and contact details of other researchers involved in this study. Please include your own name and centre if you are also a local researcher.

(Please copy and complete this page for each researcher. You must inform the LREC Administrator by means of a copy of this form as each new researcher is recruited.)

LREC Reference Number:

Name	**Dr Alison Richardson** Consultant Clinical Psychologist Research Field Supervisor	**Dr Suzanne O'Rourke** Clinical Psychologist Research Academic Supervisor
Contact Address:	Spittal Street Centre 22-24 Spittal Street Edinburgh EH3 9DU	D. Clin. Psych. Department of Psychiatry Kennedy Tower Royal Edinburgh Hospital
Location of research *(if different):*	N/A	N/A
Telephone:	0131 – 537 8300	0131 – 537 6502 or 01555 – 840293 x539

Fax:

E-Mail:

Please retain a blank copy of this form, complete it and send to the LREC Administrator whenever other local researchers become involved in the future.

Lothian NHS Board

Lothian Research Ethics Committee
Deaconess House
148 Pleasance
Edinburgh
EH8 9RS
Telephone 0131 536 9000
Fax 0131 536 9346
www.nhslothian.scot.nhs.uk

NHS Lothian

Mr John Ferguson
Studio Flat
10 Boswall Road
Trinity
Edinburgh EH5 3RH

Date 07 February 2002
Your Ref
Our Ref LREC//2002/7/6

Enquiries to Annette Harris
Extension 89050
Direct Line 0131 536 9050
Email annette.harris@lhb.scot.nhs.uk

Dear Mr Ferguson,

AN INVESTIGATION INTO HOW NORMAL AND ABNORMAL PERSONALITY CHARACTERISTICS CORRELATE WITH LEVEL OF ADHERENCE TO ANTIRETROVIRAL THERAPY IN INDIVIDUALS WITH HIV INFECTION

Thank you for submitting the above protocol for ethical approval. The Psychiatry/Clinical Psychology Research Ethics Sub-Committee will consider this protocol at its next meeting to be held on 20 February 2002. I will notify you of the outcome of this consideration as soon as possible.

Under the terms of the Scottish Office Home and Health Department Guidelines on Local Research Ethics Committees a copy of your request has been sent to the NHS body under the auspices of which the research is intended to take place. It is that NHS body which has the responsibility of deciding whether or not the research should go ahead taking account of the advice of the Research Ethics Sub-Committee and from whom you must obtain management approval before any work on the study can proceed.

Details of the Lothian Research Ethics Committee and its documentation can be found on http://www.nhslothian.scot.nhs.uk/nhs_lothian/about_lothian_health/lrec/index.html

Yours sincerely

ANNETTE HARRIS
Committee Administrator

NHS
Lothian

cc *Ms Ann Green*
c/o Nicole Tait
Level 4, Kennedy Tower
Royal Edinburgh Hospital
Edinburgh

Appendix Ib

Research protocol

NHS Lothian

Draft Research Protocol

John S Ferguson

Psychologist in Clinical Training

Full Title

Personality correlates of adherence to HIV antiretroviral therapy

Research Objectives

This study aims to profile the personality characteristics and psychosocial factors of individuals with HIV who are in receipt of antretrivoral therapy. Individual adherence profiles will also be examined in order to investigate the existence of a possible relationship between these two main variables (personality profile & level of adherence).

Additionally, further variables will be measured in terms of how they interact with both personality characteristics and adherence among HIV infected individuals. These will include gender, age, route of infection, depression/anxiety symptomatology, coping with illness and attitudes to general healthcare.

In summary, the research objective is to explicitly examine and begin to understand the role, if any, of personality and psychosocial factors in predicting level of adherence to treatment regimens. The end point of this research is to begin debating methods of improving adherence to antiretroviral therapy at an individual level.

Rationale and scientific background to the research

The proposal for this research has been born out of a literature review of those general factors considered to influence medication adherence. Most of the limited psychological research in this area cites such factors as poor social support networks, poor coping skills, dysfunctional cognitions and memory problems as indicative of poor levels of adherence. Medically driven research is widespread and appears to focus primarily on the side effects of drug therapy with antiretrovirals and the role of motivational factors in establishing a particular pattern of adherence. In HIV treatment, a high level of adherence is vital if viral suppression is to be sustained. It is clear that non-adherence is very common among patients treated for HIV infection. By understanding adherence factors in HIV, interventions can be generated and evaluated to increase treatment adherence. A running theme within the research from both disciplines is the acknowledgement of the role of personality as an inevitable influential factor in an individual's level of adherence to antiretroviral medication. Very few studies to date have expanded on this theme and research approaching possible internally-driven personality characteristics predictive of positive adherence tends to arise within the context of life-threatening illnesses in general. For example the role of motivational factors and adherence to strict therapeutic regimens has been documented in the literature in relation to conditions such as cancer, renal disease, diabetes, multiple sclerosis and hypertension (see Pyszczynski et al, 1995; Sosa et al, 1991; Zeldow et al, 1988; Oldridge & Rogowski, 1990). Personality theory would examine individual attributes in order to explain adherence. Explanations would be related to ideas such as self-efficacy, self-esteem, resilience, commitment and motivation. Personality variables may also be used to explain the extent to which the physician can present persuasive information and explanatory data thus influencing a variety of doctor-

client relationships. The doctor-client relationship has been found to be particularly important for adherence to treatment to occur.

Sherr (2000), in a review of the literature on adherence in HIV treatment, concludes that adherence can be studied from four main perspectives:

- The patient
- The preparation (or medication)
- The provider
- The place or setting

'The patient' and 'preparation' perspectives would appear to have come under most scientific scrutiny to date.

Sherr also goes on to describe how a number of psychological theories can be invoked to understand non-adherence in terms of these four levels. These include:

- Cognitive models
- Psychodynamic models
- Social concepts
- Personality concepts

Available research would appear to indicate that research has tended to apply more of a 'social' and 'cognitive' model to help explain adherence from the perspectives of the 'patient' and the 'provider'. It is the intention of this research project to apply a model of personality to the patient perspective (and to some extent the provider also) in an attempt to understand treatment adherence in antiretroviral therapy. This study is therefore being informed by previous research but with a focus on how normal personality characteristics and psychosocial indicators may or not be related to objective and subjective measures of treatment adherence.

Inherent in this research proposal is an acknowledgement that many other possible factors typically affect an individual's ability to adhere to drug regimens in HIV, as the literature clearly indicates. Such factors cannot realistically be isolated and controlled for within the limitations placed on this study. However, this proposal is also developed with a working assumption that by virtue of the natural rigidity of human personality, combined with a thorough analysis of the outcomes of both personality structure and adherence in the research sample, the study will allow meaningful inferences to be drawn about their relationship in the specific context of HIV antiretroviral therapy.

The integrity of this study is also enhanced by drawing from a well documented and contemporary biopsychosocial theory of personality developed by Theodore Millon, PhD (Davis 1999). This uniformity is further maintained by applying two personality measures, both developed by Millon, to the assessment of normal range personality and psychosocial strengths and weaknesses. These assessments, while being based upon the trait approach to personality, also take into account the cognitive and motivational aspects of individual differences. The study will examine in detail the personality styles of participants and attempt to identify correlations between various personality variables and levels of adherence to antiretroviral therapy.

Research questions and hypotheses

1. What is the overall profile of individuals on antiretroviral therapy in terms of; general personality style, attitudes to healthcare, ability coping with illness, and self-reported level of adherence? Do they differ from the normative sample?

2. What is the overall personality/psychosocial profile of individuals on antiretrovirals who may need more communication and support in order to comply with prescribed medical regimens?

3. Do particular types of profile become differentiated based upon a breakdown of objective and subjective measures of adherence? In other words based on the above variables, is there a particular profile indicative of each of the following three levels of adherence:

    - Individuals who have never reached a sustained level of therapeutic adherence
    - Individuals who have reached a sustained therapeutic level of adherence which then declined
    - Individuals who have consistently achieved a therapeutic level of adherence

4. There is no evidence for a predictable association between personality characteristics and regimen adherence in antiretroviral therapy.

5. Individuals experiencing significant personality adjustment problems do not differ from the remaining sample on measures of personality characteristics, psychosocial factors affecting attitude to healthcare, level of regimen adherence, depression and anxiety symptomatology.

6. Regimen adherence is not positively associated with anxiety and depression symptomatology.

7. Patient self-report measures of regimen adherence do not differ significantly from physiological measures of adherence.

Method

Participants:
To achieve statistical power around 70 participants will need to be recruited for this project. Individuals attending the Infectious Diseases Unit, Western General Hospital and the GUM clinic at Edinburgh Royal Infirmary will be approached with information about the study. Subject to their consent to take part, each participant will meet with the researcher and be invited to complete a small battery of questionnaires in 'pencil & paper' format.

Obtaining consent:
The following procedure will be strictly adhered in order to ensure that consent is appropriately and responsibly obtained:

- A letter will be sent to each consultant physician at the Infectious Diseases Unit/ GUM Dept. requesting consent to approach his or her patients with regard to taking part in the study. Each consultant will also be sent an information sheet explaining the objectives and methodology of the project.
- Pending their own consent to approach and recruit patients, each consultant will then distribute a further information sheet to each patient within a letter inviting them to take part and to obtain the direct consent of each patient (including consent to view case notes).
- Additional consent will be sought from consultants in order to approach in-patients and information sheets will be distributed to nursing staff and throughout in-patient wards.

Outcome measures:
The battery of assessments will consist of:

- A short demographic questionnaire
- A brief self-report questionnaire on treatment adherence
- The Millon Index of Personality Styles (MIPS)
- The Millon Behavioural Medicine Diagnostic (MBMD)

It is estimated that the entire assessment battery will take 1hr – 1hr 15mins. to complete. The researcher will be present during completion of the assessment.

The MIPS is designed for use by professionals looking for a comprehensive, well-rounded report of general personality. It is a standardised psychological assessment containing 180 unobtrusive True/False items organised into 3 groups of scales, together with 3 validity indicators or response sets: Motivating Aims, Interpersonal Behaviours, Cognitive Modes, Response Sets. The MBMD was developed to aid clinicians including consultant physicians and clinical/health psychologists who work with physically ill and behavioural medicine patients. The test aids in the psychological understanding of these patients. The MBMD can help pinpoint personal and social assets that may facilitate adjustment to lifestyle changes. It can also help identify individuals who may need more communication and support on order to adhere to treatment regimens. It is a standardised instrument that assesses negative health habits, psychiatric indicators, coping styles, stress moderators, treatment prognostics and adjustment difficulties. The MBMD norms are based on extended research with patients with a wide variety of medical conditions including HIV/AIDS. It consists of 165 True/False items grouped into 38 content scales. Both tests draw from Dr T. Millon's widely accepted theory of personality.

Design:
The study is cross-sectional in design. Concurrent with a structured personality assessment the researcher will also consult a computerised database of patient information located at the Infectious Diseases Unit, Western General Hospital. This database will reveal the level of adherence of each patient according to frequency of inpatient visits and viral load over time (a physiological marker of adherence to treatment). Correlations between personality variables and level of treatment adherence will be examined upon statistical analysis of the data. Multiple regression will be used for statistical analysis in order to examine the extent to which levels of regimen adherence (dependent variable), is predictable from variations in demographics, anxiety, depression, psychosocial indicators, and a range of personality characteristics and clinical personality pathology.

References

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01.03.02

Appendix Ic

Research participant information sheet

NHS Lothian

Patient Information Sheet

25th March 2002

Researcher: John Ferguson
Psychologist in Clinical Training
Doctorate in Clinical Psychology
University of Edinburgh/
East of Scotland Health Boards
Training Course in Clinical Psychology
Kennedy Tower, Royal Edinburgh Hospital
Morningside Park, Edinburgh
EH10 5HF
Tel: 0131-537 8300
0131-537 6279

Dear Sir/Madam

The role of individual personality characteristics in predicting levels of therapeutic adherence to antiretroviral therapy

I would like to invite you to take part in a research study that aims to explore the role of personality in determining how well individuals manage to adhere to antiretroviral treatment for HIV.

Before you decide whether or not you wish to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Your consultant has given permission for me to approach you with this information. Please contact me if there is anything that is not clear, or if you would like more information. Take time to decide whether or not you wish to take part.

Thank you for reading this.

Why is the study taking place?

- Non-adherence is very common among patients treated for HIV infection. During treatment it is already known that a high level of adherence to antiretroviral therapy is vital if viral suppression is to be sustained. Research has shown that many factors may influence treatment adherence. Not much is known about the role of personality factors. By understanding how personality may or may not affect adherence, it may be possible to help people adhere to antiretroviral therapy more effectively.

What is the purpose of the study?

- To provide a profile of people on antiretroviral therapy in terms of general personality characteristics and to investigate if there is any relationship between these characteristics and a person's ability to adhere successfully to treatment.
- The study is taking place between March and August 2002.

Why have I been chosen?
You have been invited to take part in this research because you are currently receiving antriretroval therapy and have direct experience of the difficulties involved in managing your medication. You also attend regular reviews at the Western General Hospital and it might be convenient for you to take part in this Edinburgh based study.

Do I have to take part?
No. It is entirely up to you whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. By signing the consent form you are agreeing to take part in the study and also giving the researcher permission to view your medical records held by the hospital.

What will happen to me if I take part?
Once you have returned your consent form to the researcher, the researcher will contact you by letter to offer an appointment to meet in order to complete the following questionnaires:

- A short questionnaire relating to your gender, age, route of HIV infection etc
- A questionnaire relating to how well you think you adhere to treatment
- A questionnaire relating to your particular personality style
- A questionnaire relating to your general health, how you cope with stress & illness, and your attitudes to issues of your general healthcare

These questionnaires should take approximately 1hr – 1hr 15 mins. to complete. The questions are short and will mostly only require 'true/false' answers.

Are there any disadvantages in taking part?
There should be no ill effects in taking part in this study. However, some people do experience discomfort when responding to questionnaires about themselves. It is unlikely that this will be the case. However, if you have any questions about the study and wish to discuss them then please do not hesitate to contact me.

Confidentiality
All information you give about yourself during the course of this research will be strictly confidential. Any information about you which leaves the hospital will have your name removed so that you cannot be identified from it. The consent form will be kept separately from the completed questionnaires and you will be allocated an individual participant number to ensure anonymity. You will not be identified in any subsequent report or publication as a result of this research study.

Withdrawal
Your participation in this research is entirely voluntary. If you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect any of the care you receive.

What will happen with the results?
A detailed summary of the research results and implications will be sent to your consultant for their interest. If interested you will be able to receive a copy of the results from either the researcher or your consultant after September 2002.

Further Information
If you require any further information about the study, or have any questions or comments, please feel free to contact me.

Thank you very much for taking the time to consider and/or participate in this research

If you wish to take part please sign and return the enclosed consent form in the envelope provided

Yours sincerely

John Ferguson
Psychologist in Clinical Training
Doctorate in Clinical Psychology
University of Edinburgh

Supervised by:

Dr Alison Richardson
Consultant Clinical Psychologist
Research Field Supervisor

Dr Suzanne O'Rourke
Clinical Psychologist
Research Academic Supervisor

Appendix Id

Research participant consent form

NHS Lothian

Consent Form

Title of Project:

The role of individual personality characteristics in predicting levels of therapeutic adherence to antiretroviral therapy

Name of Researcher: Mr John Ferguson

1. I confirm that I have read and understood the information sheet which I have been given about this research study.

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.

3. I understand that sections of my medical notes may be looked at by the researcher where it is relevant to my taking part in this research. I give permission for the above named researcher to have access to my records.

4. I agree to take part in the above research study.

It would be preferable to contact you by telephone to arrange a time to meet.

If possible please enter your contact number .....

Please also sign & print your name below:

....
Signature of Patient **Date**

.....
Printed Name of Patient

....
Signature of Person taking consent (if different from researcher) Date

.....
Printed Name of Person taking consent

....
Signature of Researcher Date

Appendix Ie

Consultant information sheet

Lothian Primary Care NHS Trust

NHS
Lothian

12th March 2002

Dr
Regional Infectious Diseases Unit
Western General Hospital
Edinburgh

Researcher: John Ferguson
Psychologist in Clinical Training
Doctorate in Clinical Psychology
University of Edinburgh/
East of Scotland Health Boards
Training Course in Clinical Psychology
Kennedy Tower, Royal Edinburgh Hospital
Morningside Park, Edinburgh
EH10 5HF
Tel: 0131-537 8300
0131-537 6279

Dear

I write to ask if you may consider approaching your patients regarding a research study I am undertaking. The research will examine **the relationship between personality characteristics / psychosocial factors and level of adherence to antiretroviral therapy**. The study will be presented as a thesis in part fulfilment of the degree of Doctorate in Clinical Psychology at the University of Edinburgh. I am a final year trainee clinical psychologist on a specialist year-long placement with Dr Alison Richardson at the Spittal Street Centre.

I would be grateful if you could approach your patients to determine if they would be interested in opting to participate in the study.

For your information I enclose a research protocol which outlines the objectives and methodology behind my proposed piece of research.

I require a sample of participants who fulfil the following inclusion criteria:

Individuals who have HIV positive status and are currently in receipt of antiretroviral medication or have been on antiretrovirals and in attendance at the Infectious Diseases Unit within the last six months.

I also enclose patient information leaflets and consent forms for you to distribute to your patients to facilitate their decision whether or not to participate. Once an individual opts in by returning their consent form to me, I will then approach them by letter with the offer of an appointment to meet and complete the measures involved in the research.

I am very grateful for your consideration of this. Please do not hesitate to contact me if you would like any further information. I look forward to hearing from you in the near future regarding this project.

Yours sincerely

John Ferguson
Psychologist in Clinical Training

Supervised by:

Dr Alison Richardson
Consultant Clinical Psychologist
Research Field Supervisor

Dr Suzanne O'Rourke
Clinical Psychologist
Research Academic Supervisor

Mr Mike Henderson
Independent Adviser
Clinical Tutor/D. Clin. Psych. Training course, Edinburgh

C.c.

For Consultant information:	Research Protocol
For Patient Information:	Information Sheet Consent Form Return Envelope

NHS
Lothian

25th March 2002

Dr G R Scott
Consultant Physician
Dept of G U Medicine
Level 1, Lauriston Building
The Royal Infirmary Edinburgh

Researcher: John Ferguson
Psychologist in Clinical Training
Doctorate in Clinical Psychology
University of Edinburgh/
East of Scotland Health Boards
Training Course in Clinical Psychology
Kennedy Tower, Royal Edinburgh Hospital
Morningside Park, Edinburgh
EH10 5HF
Tel: 0131-537 8300
0131-537 6279

Dear Dr Scott

I write to ask if you may consider approaching your patients regarding a research study I am undertaking. The research will examine **the relationship between personality characteristics / psychosocial factors and level of adherence to antiretroviral therapy**. The study will be presented as a thesis in part fulfilment of the degree of Doctorate in Clinical Psychology at the University of Edinburgh. I am a final year trainee clinical psychologist on a specialist year-long placement with Dr Alison Richardson at the Spittal Street Centre.

I would be grateful if you could approach your patients to determine if they would be interested in opting to participate in the study.

For your information I enclose a research protocol which outlines the objectives and methodology behind my proposed piece of research.

I require a sample of participants who fulfil the following inclusion criteria:

Individuals who have HIV positive status and are currently in receipt of antiretroviral medication or have been on antiretrovirals and in attendance at the Dept. of G U Medicine within the last six months.

I also enclose sample patient information leaflets and consent forms for your perusal. Once an individual opts in by returning their consent form to me, I will then approach them by letter with the offer of an appointment to meet and complete the measures involved in the research. Upon your consent, I will contact you again shortly in order to supply information packs for distribution to your patients. I have already begun distributing same information to the medics at RIDU.

I am very grateful for your consideration of this. Please do not hesitate to contact me if you would like any further information. I look forward to hearing from you in the near future regarding this project.

Yours sincerely

John Ferguson
Psychologist in Clinical Training

Supervised by:

Dr Alison Richardson
Consultant Clinical Psychologist
Research Field Supervisor

Dr Suzanne O'Rourke
Clinical Psychologist
Research Academic Supervisor

Mr Mike Henderson
Independent Adviser
Clinical Tutor/D. Clin. Psych. Training course, Edinburgh

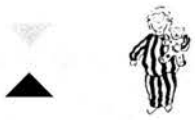
C.c.

For Consultant information: Research Protocol
Patient Information Sheets
Consent Form

Appendix If

Written consent from consultants

The Lothian University Hospitals NHS Trust



THE ROYAL INFIRMARY OF EDINBURGH
Lauriston Place, Edinburgh EH3 9YW

Dept of G U Medicine
Level 1, Lauriston Building
Tel: 0131 536 2098

Mr John Ferguson
Clinical Psychology Student
HARM Reduction Team
The Spittal Street Centre
22-24 Spittal Street
EDINBURGH

GRS/CE
22 March 2002

Dear John

With regard to your research on adherence to HIV medication, I have had a request from the R & D Department in the Trust to send a letter giving my agreement to you undertaking research with our patients. This is fine, but I have managed to mislay the letter that you sent me about the study. Could you please give me a few details and I shall send a formal letter to the Trust.

Kind regards.

Yours sincerely

G R SCOTT FRCP
Consultant Physician

The Lothian University Hospitals NHS Trust

THE ROYAL INFIRMARY OF EDINBURGH
Lauriston Place, Edinburgh EH3 9YW

Dept of G U Medicine
Level 1, Lauriston Building
Tel: 0131 536 2098

CONFIDENTIAL

GRS/CE

4 April 2002

Alison Craig
Research & Development Department
RIE

Dear Alison

Research Study On The Relationship Between Personality Characteristics/Psychosocial Factors and Level of Adherence to Antiretroviral Therapy

I have reviewed the application for this research study, and am happy to confirm that we give permission for our patients to be approached to participate in this study.

Kind regards.

Yours sincerely

G R SCOTT FRCP
Consultant Physician

cc. John Ferguson, Psychologist in Clinical Training, Kennedy Tower, Royal Edinburgh Hospital.

Appendix Ig

Notification of approval by research & development office

ROYAL INFIRMARY OF EDINBURGH
1 Lauriston Place, Edinburgh, EH3 9YW

RESEARCH & DEVELOPMENT OFFICE (Ward 47)

Tel:/ Fax 0131 536 3420
Email
glynis.omond@luht.scot.nhs.uk

Director:
Dr Heather A Cubie
FRCPath

R&D Manager:
Rachel Smith
PhD

Commercial Research Manager:
Douglas Young
PhD MBA

Accountant:
Ms Sheevaun McIntyre
BAcc

Information Officer:
Lena Kelly
RGN BSc (Hons)

PA/Office Manager:
Mrs Glynis Omond

Administrative Assistant:
Mr Neil Feltham

Divisional Admin Officers:
Medical
Alison Clark
RGN BSc (Hons)
Surgical
Mr Patrick Stevenson
MA (Hons)
Women & Children / Clinical Support
Dr Rhian Hunter

HAC/GO/app1a/patnoncomm

10 April 2002

Dr RP Brettle
Regional Infectious Diseases Unit
Western General Hospital
Crewe Road

Dear Dr Brettle

LREC No:	**2002/7/6**
R&D Project ID No:	**2001/W/ID/11**
Title of Research	*An investigation into how normal and abnormal personality characteristics correlate with level of adherence to antiretroviral therapy in individuals with HIV infection*

The above project has undergone a review of resource and financial implications by the R&D Office and I am satisfied that all the necessary arrangements have been set in place.

On behalf of the Trust Chief Executive and Medical Director, I am happy to give Trust management approval to allow the project to commence, subject to the approval of the appropriate Research Ethics Sub-Committee having also been obtained.

We would ask you to note that under Section 7, question 34, The Lothian University Hospitals NHS Trust provides indemnity for negligence for NHS and honorary clinical staff wherever research involves patients attending the hospitals. It is not empowered to provide non negligent indemnity for patients or volunteers.

Yours sincerely

Dr Heather A Cubie
R&D Director

cc *Secretary, Research Ethics Sub-Committee*
Mr John Ferguson, Psychologist in Clinical Training, Kennedy Tower, Royal Edinburgh Hospital

Appendix Ih

Research ethics sub-committee amendments

Lothian NHS Board

Lothian Research Ethics Committee
Deaconess House
148 Pleasance
Edinburgh
EH8 9RS
Telephone 0131 536 9000
Fax 0131 536 9346
www.nhslothian.scot.nhs.uk

NHS Lothian

Mr John Ferguson
Studio Flat
10 Boswall Road
Trinity
Edinburgh EH5 3RH

Date 26 February 2002
Your Ref
Our Ref LREC//2002/7/6

Enquiries to Annette Harris
Extension 89050
Direct Line 0131 536 9050
Email annette.harris@lhb.scot.nhs.uk

Dear Mr Ferguson,

AN INVESTIGATION INTO HOW NORMAL AND ABNORMAL PERSONALITY CHARACTERISTICS CORRELATE WITH LEVEL OF ADHERENCE TO ANTIRETROVIRAL THERAPY IN INDIVIDUALS WITH HIV INFECTION

Thank you for submitting the above protocol for ethical approval. The Psychiatry/Clinical Psychology Research Ethics Sub-Committee has discussed this protocol and has agreed that it is prepared to grant ethical approval subject to the following amendments, delegating authority to the Chairman to approve them on receipt:

- The signature of the independent adviser is required
- The initial approach to patients asking them if they are interested in being approached by the researcher, must be made by the consultant in charge of their clinical care. Patients must opt to participate in the study before being contacted by the researcher and this should be reflected in the letter from the consultant.

Once these amendments have been received by me and approved by the Chairman a formal Certificate of Approval will be issued. Only then can management approval be given and the research proceed.

The next meeting of the Sub-Committee will be held on 20 March 2002. It would be appreciated if the required amendments could be available prior to that date.

NHS
Lothian

Should you have any queries regarding the above, please contact myself on the number below.

Details of the Lothian Research Ethics Committee and its documentation can be found on http://www.nhslothian.scot.nhs.uk/nhs_lothian/about_lothian_health/lrec/index.html

Yours sincerely

ANNETTE HARRIS
Committee Administrator

cc *Ms Ann Green*
c/o Nicole Tait
Level 4, Kennedy Tower
Royal Edinburgh Hospital
Edinburgh

Lothian Primary Care NHS Trust

NHS
Lothian

Annette Harris
LREC
Deaconess House
148 Pleasance
Edinburgh
EH8 9RS

John Ferguson
Harm Reduction Team
Spittal Street Centre
22-24 Spittal Street
Edinburgh
EH3 9DU

Dear Annette

I was sorry to hear that you had not received these amendments already. However I now enclose them again and also copy to Mr Neil Feltham (R&D, Edinburgh Royal Infirmary) who has requested the same information for his records.

Please do contact me if there is any further information that you require, and many thanks for your consideration of my proposal.

Yours Sincerely

John Ferguson
Psychologist in Clinical Training

C.c. Mr Neil Feltham
R&D Office
Ward 71
Edinburgh Royal Infirmary

Appendix Ii

Official certificate of ethical review

Lothian NHS Board

Lothian Research Ethics Committee
Deaconess House
148 Pleasance
Edinburgh
EH8 9RS
Telephone 0131 536 9000
Fax 0131 536 9346
www.nhslothian.scot.nhs.uk

NHS Lothian

Mr John Ferguson
Studio Flat
10 Boswall Road
Trinity
Edinburgh EH5 3RH

Date 12 April 2002
Your Ref
Our Ref LREC//2002/7/6

Enquiries to Annette Harris
Extension 89050
Direct Line 0131 536 9050
Email annette.harris@lhb.scot.nhs.uk

Dear Mr Ferguson,

AN INVESTIGATION INTO HOW NORMAL AND ABNORMAL PERSONALITY CHARACTERISTICS CORRELATE WITH LEVEL OF ADHERENCE TO ANTIRETROVIRAL THERAPY IN INDIVIDUALS WITH HIV INFECTION

Thank you for submitting the amendments or additional information requested by the Sub-Committee for the above protocol. The Chairman of the Psychiatry/Clinical Psychology Research Ethics Sub-Committee has now agreed to confirm the Sub-Committee's ethical approval under its delegated authority. An official Certificate of Ethical Review is enclosed together with a list of members present at the meeting.

Under the terms of the Scottish Office Home and Health Department Guidelines on Local Research Ethics Committees this decision has been notified to the NHS body under the auspices of which the research is intended to take place. It is that NHS body which has the responsibility of deciding whether or not the research should go ahead taking account of the advice of the Research Ethics Sub-Committee and from whom you must obtain management approval before any work on the study can proceed.

Details of the Lothian Research Ethics Committee and its documentation can be found on http://www.nhslothian.scot.nhs.uk/nhs_lothian/about_lothian_health/lrec/index.html

Yours sincerely

ANNETTE HARRIS
Committee Administrator

NHS
Lothian

cc *Ms Ann Green*
c/o Nicole Tait
Level 4, Kennedy Tower
Royal Edinburgh Hospital
Edinburgh

PSYCHIATRY/CLINICAL PSYCHOLOGY
RESEARCH ETHICS SUB-COMMITTEE

Wednesday 20 February 2002

Present

Dr A Richardson (Consultant Psychologist) (Chairman)
Mr J Oliphant (Nursing Member)
Mr R Beasley (Lay Member)
Dr D Morrison (Consultant Psychiatrist)
Dr I McKee (GP Representative)
Ms F Barry (Consultant Psychologist)
Mr N Grier (Lay Member)
Dr T White (Consultant Psychiatrist)

LOTHIAN RESEARCH ETHICS COMMITTEE

CERTIFICATE OF ETHICAL REVIEW

LREC Reference Number: LREC/2002/7/6
Title: An investigation into how normal and abnormal personality characteristics correlate with level of adherence to antiretroviral therapy in individuals with HIV infection
Researcher: Mr John Ferguson

The Psychiatry/Clinical Psychology Research Ethics Sub-Committee reviewed this proposed study and has agreed that it is ethical and appropriate to be carried out in the Lothian Area. This opinion encompasses all aspects of the application including the Patient/Subject Information Sheet and all other accompanying documentation provided.

The LREC application form, protocol, subject information sheet, information on compensation arrangements, payments to researchers and the provision of expenses to subjects (where appropriate) were reviewed and approved.

The membership of the Psychiatry/Clinical Psychology Research Ethics Sub-Committee is shown on the attached sheet.

It is a condition of this opinion that you **must** obtain appropriate management approval from the relevant NHS body under the auspices of which the research is intended to take place **before** starting the study. It is that NHS body which has the responsibility of deciding whether or not the research should go ahead taking account of the advice of the Local Research Ethics Committee. It is also a condition that you are required to notify the Psychiatry/Clinical Psychology Research Ethics Sub-Committee **and** the relevant NHS body, in advance, of any significant proposed deviation from the original protocol or application form. Reports to the Sub-Committee and the relevant NHS body are also required once the research is underway if there are any unusual or unexpected results which raise questions about the safety of the research.

Researchers are also required to report on success, or difficulties, in recruiting subjects in order to provide useful feedback on perceptions of the project among patients and volunteers.

Peter Reith
Secretary
Lothian Research Ethics Committee

Annette Harris
Administrator
Psychiatry/Clinical Psychology
Research Ethics Sub-Committee

12 April 2002

The Psychiatry/Clinical Psychology Research Ethics Sub-Committee is fully compliant with the International Committee on Harmonisation/Good Clinical Practice (ICH) Guidelines for the Conduct of Trials Involving the Participation of Human Subjects as they relate to the responsibilities, composition, function, operations and records of an Independent Ethics Committee/Independent Review Board. To this end it undertakes to adhere as far as is consistent with its Standing Orders, to the relevant clauses of the ICH Harmonised Tripartite Guideline for Good Clinical Practice, adopted by the Commission of the European Union on 17 January 1997. The Membership List, Standing Orders and Statement of Compliance were included on the computer disk containing the guidelines and application form and are available on request.

Appendix II

Socio-demographic and adherence self-report questionnaire

Demographic Questionnaire

Participant No:

Gender

Male	1.
Female	2.

DOB:

Employment Status

Full Time	1.
Part Time	2.
Unemployed	3.
Voluntary Worker	4.

Age

18 – 25	1.
26 – 35	2.
36 – 45	3.
46 – 55	4.
56 – 65	5.
>65	6.

Sexual Orientation

Heterosexual	1.
Homosexual	2.
Bisexual	3.

Marital Status

Single	1.	Widowed	4.
Married	2.	Cohabiting	5.
Divorced	3.		

Route of HIV Infection

Sexual Transmission	1.
Sharing Needles/Equipment	2.
Blood Transfusion	3.
Use of Blood Products	4.
Organ Transplant	5.
Needlestick Injury	6.
Unknown	7.

Date of HIV Diagnosis:

AIDS Diagnosis? Yes 1. No 2.

Illegal Drug Use

Heroin	1.	Cocaine	7.
DHC	2.	Crack	8.
Other Opiate	3.	Amphetamine	9.
Diazepam	4.	LSD	10.
Temazepam	5.	MDMA etc	11.
Other Benzo	6.	Cannabis	12.
		Other	13.

Previous Drug Use? _____

Legal Prescription Drug Use

Yes 1. No 2.

List: 1. _____

2. _____

3. _____

4. _____

Alcohol Use

Yes 1. No 2.

No. Units Per Week :

Permission for Medical Notes to be consulted for test results.

Yes 1. No 2.

Adherence Questionnaire

Knowledge of Cell CD4 Counts

Note:

Knowledge of Viral Load

Note:

Currently Receiving Antiretroviral Therapy? Yes 1. No 2.

If No – Why Not?

Note:

Frequency

Current Course of Antiretrovirals	**1** x 2 daily	**2** x 3 daily	**3** x 2 daily with meals	**4** x 3 daily with meals	**5** x 2 daily 1 or 2 hours before or after meals	**6** x 3 daily 1 or 2 hours before or after meals	**7** Other
List: 1. _____							
2. _____							
3. _____							
4. _____							
5. _____							

How many tablets do you/did you take each day?

Are you taking them at all? Yes 1. No 2.

If No – why not?

Note:

In the last month have you missed any doses?

Yes 1. No 2.

How often have you missed a dose?

> 1 per day	1.
> 1 per week	2.
> 1 per month	3.
Other	4.

What are your reasons for missing these doses?

List: 1. _____

2. _____

3. _____

4. _____

5. _____

Do you suffer any drug-related side effects?

Yes 1.
No 2.

If Yes – what?

List:

Do you ever take any of the drugs at a different time specified? Yes 1. No 2.

If so – how often per week?

Do you stick to the advice about food? Yes 1. No 2.

If not – how often per week?

What are your reasons for taking Combination Therapy?

List:

What do you think about Combination Therapy?

What do you understand about resistance to antiretrovirals?

Why is it important to adhere to treatment?

Viral Load

Now _____

Highest Ever _____

CD4 Count

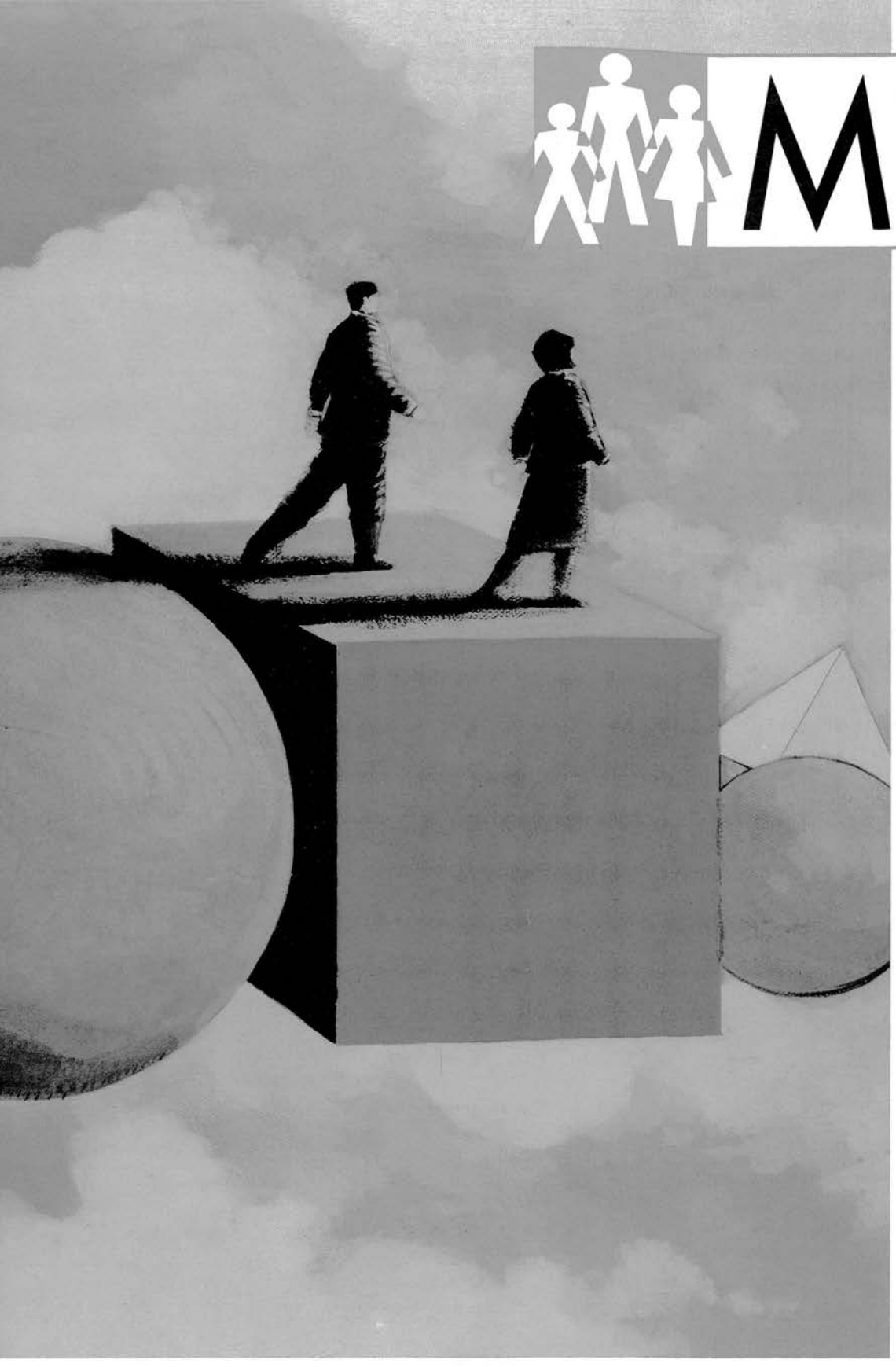
Now _____

Lowest Ever _____

Appendix III

Millon Index of Personality Styles

Test Booklet



MIPS™

Test Booklet

THE PSYCHOLOGICAL CORPORATION®
Harcourt Brace & Company
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015-454163X

MIPS™

Directions: The following pages contain a list of statements. Read each statement and decide whether or not it describes you. If you agree with a statement or believe that it is true about you, blacken the *T* circle for *true* on the Answer Sheet. If you disagree with a statement or believe that it is not true about you, blacken the *F* circle for *false* on the Answer Sheet. Be sure to answer either true or false for every statement. There are no *right* or *wrong* answers.

1 I am a quiet and cooperative person.
2 I have always done things my way and taken the consequences.
3 I like to be the one to take charge.
4 I have always had a regular way of doing things so I can avoid mistakes.
5 I respond the same day to letters I get.
6 Every now and then I ruin the good things that happen to me.
7 I don't get excited about much any more.
8 I would much rather be a follower than be a leader.
9 I go out of my way to make myself popular with others.
10 I have always had a talent for being successful.

11 I often find that I've been treated unfairly.
12 I feel uncomfortable when people are good to me.
13 I often feel self-conscious and tense at social gatherings.
14 Police take too much advantage of the power they have.
15 Sometimes I have had to be pretty rough with people.
16 Children should always obey the rules of their elders.
17 I often feel disgusted with the way things are going.
18 I often expect the worst to happen to me.
19 I wouldn't mind not having many friends.
20 I am a shy and socially inhibited person.

21 Even when I disagree, I usually let others have their way.
22 No one should be expected to always tell the truth.
23 I make nasty remarks to people if they deserve them.
24 I like to follow instructions and do what others expect of me.
25 So little of what I do is appreciated by others.
26 Almost anything I try is easy for me.
27 I've become more drawn into myself in recent years.
28 I am a dramatic and showy sort of person.
29 I always try to do what is proper.
30 I don't depend much on other people for friendship.

31 I've never overstayed my time at a parking meter.
32 Punishment hasn't stopped me from doing whatever I wanted.
33 I like to arrange things to the last detail.
34 I am often annoyed by others.
35 I never broke any rule my parents expected me to follow.
36 I get what I want even if I have to bully others.
37 Nothing is more important than protecting one's moral reputation.
38 Opportunities don't work out for me the way they do for others.
39 I don't show much feeling any more.
40 What I have to say is not likely to interest others.

41 I go out of my way to meet exciting people and to have adventures.
42 I don't take many of my responsibilities too seriously.
43 I'm a tough, unsentimental sort of person.
44 Few things in life seem to stir me very much.
45 I become very tense when I have to talk to people I don't know.
46 I'm a cooperative person who gives in to others.
47 I like to act on the spur of the moment.
48 I think ahead and then actively follow through.
49 I have often been restless and wanted to move on to almost anywhere else.
50 It is best to tightly control one's emotions.

51 I wish people would not blame me when things go wrong.
52 I'm probably my own worst enemy.
53 I have very few close ties with others.
54 I feel anxious with people I don't know very well.
55 It's all right to get around the law, if you don't break it.
56 I do a lot for others, but little is done for me.
57 I've always believed that others don't think well of me.
58 I am very confident.

59 I very systematically arrange my papers and records.
60 From past experience I know that good things don't last.

61 Some people say I enjoy being a martyr.
62 I am most comfortable when I'm alone.
63 I become much more tense than others do in new situations.
64 I always try to avoid disagreements, no matter how strongly I feel about the subject.
65 I look for opportunities that are exciting and new to me.
66 There were times when my parents had trouble keeping me in line.
67 I always finish my work before I relax.
68 Others get breaks I don't get.
69 I sometimes feel I deserve to be unhappy.
70 I wait for events to take their course before deciding what to do.

71 I try to take care of others before I take care of myself.
72 I often feel that my life goes from bad to worse.
73 I am inspired simply by being around people.
74 I always check the speed limit and never drive faster than what's posted.
75 I use my head, not my heart, to make decisions.
76 I usually follow my hunches, not the information I may have.
77 I'm never envious of the achievement of others.
78 I preferred school subjects that were factual rather than theoretical.
79 I plan ahead and then act decisively to make my plans happen.
80 My heart seems to rule my head.

81 I can always see the bright side of life.
82 I often wait for someone else to solve my problems.
83 I do what I want without worrying about the effects on others.
84 I react quickly to anything that might become a problem to me.
85 I feel good about myself only when I'm helpful to others.
86 When something little goes wrong, my whole day can be spoiled.
87 I enjoy daydreams more than everyday realities.
88 I'm content to sit back and let life take its course.
89 I try to be logical rather than emotional.
90 I prefer things that I can see and touch rather than things I just imagine.

91 Talking with someone whom I've just met is difficult.
92 Being kindhearted is much more important than being cool and logical.
93 Guesses about the future are more interesting to me than facts about the past.
94 It's very easy for me to enjoy myself.
95 I don't seem able to influence the world around me.
96 I live in terms of my own needs, not the needs of others.
97 I never wait for things to happen; I make them happen my way.
98 I never voice a curse-word even when I'm furious with someone.
99 My life is guided by a need to help others.
100 I often feel on edge, waiting for something to go wrong.

101 Even when I was a youngster I would never cheat on a test.
102 I am always cool and objective when dealing with others.
103 I'd rather learn how to run a machine than speculate on why it works.
104 I'm not an easy person to get to know.
105 I spend a lot of time thinking about the mysteries of life.
106 I cope very easily with emotional ups and downs.
107 I am somewhat passive and slow about organizing my life.
108 I do what I want without worrying about pleasing others.
109 No matter what the temptation may be, I would never do something wrong.
110 Friends and family turn to me first for warmth and support.

111 Even when life is going well, I usually expect it will soon get worse.
112 I carefully plan and organize my work before I begin.
113 I am impersonal and objective when I try to solve a problem.
114 I am a realistic person who does not like to speculate about things.
115 Some of my best friends don't know how I really feel.
116 Others consider me cool-headed rather than warmhearted.
117 My sense of reality is better than my sense of imagination.
118 I look out for myself first and then think of others.
119 I spend a lot of effort to see that life works out well for me.
120 I always keep my composure, no matter what's happening.

121 I show a great deal of warmth toward my friends.
122 Very few things have worked out well for me.
123 I like to meet new people and learn about their lives.
124 I can ignore personal and emotional matters in my work.
125 I prefer to deal with realities, not with possibilities.
126 I seem to need a lot of time to be alone with my thoughts.
127 Feelings of the heart are of greater value than the logic of the mind.
128 I like dreamers more than I do realists.
129 I'm able to laugh at problems more easily than most people are.
130 There's not much I can do, so I just wait to see what happens.

131 I never get into arguments, no matter how angry I am.
132 I express my thoughts openly and freely.
133 I look at the job to be done, and not at the feelings of the people involved.
134 Working on creative ideas would be ideal for me.
135 I'm the kind of person who takes life easy and prefers to watch the passing scene.
136 I dislike depending on anyone in my work.
137 I see to it that things come out the way I want them to.
138 I enjoy everyday realities more than daydreams.
139 Lots of small things upset me.
140 I learn best by watching and talking to people.

141 I'm not content to sit back and let life take its course.
142 Meeting new people is not something I look forward to.
143 I seldom know how to keep a social conversation going.
144 I always take others' feelings into account.
145 I trust my hunches more than my observations.
146 I tend not to act until I know what others are going to do.
147 I prefer to make decisions on my own, with little or no advice from others.
148 I often feel miserable for no good reason.
149 I like being popular and doing lots of social activities.
150 I rarely express my inner thoughts to others.

151 I am enthusiastic about almost all of the activities I do.
152 I make it a practice to depend on myself and not on others.
153 Most of the time I'm actively involved in arranging the events in my life.
154 There's nothing like the warm feeling of being with a group of relatives.
155 Sometimes I am tense or depressed, and I don't know why.
156 I really enjoy discussions about myths and mystical events.
157 I decide my priorities and then take firm action to achieve them.
158 I don't hesitate to direct people to do what I think is best for them.
159 I'm proud that I am efficient and organized.
160 I really dislike people who become leaders for no good reason.

161 I am ambitious.
162 I know how to charm people.
163 Others can always rely on me to do my work diligently.
164 Others consider me warmhearted rather than cool-headed.
165 I'd be willing to work for years to become someone of importance.
166 I would enjoy selling new ideas or products to people.
167 I usually persuade others to do exactly what I want them to do.
168 I enjoy work that requires careful attention to details.
169 I'm very introspective, always trying to understand my thoughts and emotions.
170 I have great confidence in my social abilities.

171 I quickly size up situations and then act to make them turn out the way I want.
172 I can persuade almost anyone to switch to my side of an argument.
173 I will get any job done no matter what the obstacles may be.
174 Like a good salesperson, I can successfully influence people in a socially pleasing manner.
175 Meeting new people is something I look forward to.
176 The welfare of those affected should be the primary consideration when a decision about them is made.
177 I have the patience to attend to work that must be highly accurate.
178 My sense of imagination is better than my sense of reality.
179 I'm motivated to become one of the best in my field.
180 I have a pleasing social style that makes people easily like me.

Appendix IV

Millon Index of Personality Styles

Answer Sheet

MIPS™

Answer Sheet

Name _____

Date of Birth ___/___/___ Date ___/___/___

Gender _____

Marital Status _____

Race/Ethnicity _____

ID _____

Occupation _____

Education _____

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Printed in the United States of America.

015-4541648 7 8 9 10 11 12 A B C D E

1	Ⓣ	Ⓕ	41	Ⓣ	Ⓕ	81	Ⓣ	Ⓕ	121	Ⓣ	Ⓕ	161	Ⓣ	Ⓕ
2	Ⓣ	Ⓕ	42	Ⓣ	Ⓕ	82	Ⓣ	Ⓕ	122	Ⓣ	Ⓕ	162	Ⓣ	Ⓕ
3	Ⓣ	Ⓕ	43	Ⓣ	Ⓕ	83	Ⓣ	Ⓕ	123	Ⓣ	Ⓕ	163	Ⓣ	Ⓕ
4	Ⓣ	Ⓕ	44	Ⓣ	Ⓕ	84	Ⓣ	Ⓕ	124	Ⓣ	Ⓕ	164	Ⓣ	Ⓕ
5	Ⓣ	Ⓕ	45	Ⓣ	Ⓕ	85	Ⓣ	Ⓕ	125	Ⓣ	Ⓕ	165	Ⓣ	Ⓕ
6	Ⓣ	Ⓕ	46	Ⓣ	Ⓕ	86	Ⓣ	Ⓕ	126	Ⓣ	Ⓕ	166	Ⓣ	Ⓕ
7	Ⓣ	Ⓕ	47	Ⓣ	Ⓕ	87	Ⓣ	Ⓕ	127	Ⓣ	Ⓕ	167	Ⓣ	Ⓕ
8	Ⓣ	Ⓕ	48	Ⓣ	Ⓕ	88	Ⓣ	Ⓕ	128	Ⓣ	Ⓕ	168	Ⓣ	Ⓕ
9	Ⓣ	Ⓕ	49	Ⓣ	Ⓕ	89	Ⓣ	Ⓕ	129	Ⓣ	Ⓕ	169	Ⓣ	Ⓕ
10	Ⓣ	Ⓕ	50	Ⓣ	Ⓕ	90	Ⓣ	Ⓕ	130	Ⓣ	Ⓕ	170	Ⓣ	Ⓕ
11	Ⓣ	Ⓕ	51	Ⓣ	Ⓕ	91	Ⓣ	Ⓕ	131	Ⓣ	Ⓕ	171	Ⓣ	Ⓕ
12	Ⓣ	Ⓕ	52	Ⓣ	Ⓕ	92	Ⓣ	Ⓕ	132	Ⓣ	Ⓕ	172	Ⓣ	Ⓕ
13	Ⓣ	Ⓕ	53	Ⓣ	Ⓕ	93	Ⓣ	Ⓕ	133	Ⓣ	Ⓕ	173	Ⓣ	Ⓕ
14	Ⓣ	Ⓕ	54	Ⓣ	Ⓕ	94	Ⓣ	Ⓕ	134	Ⓣ	Ⓕ	174	Ⓣ	Ⓕ
15	Ⓣ	Ⓕ	55	Ⓣ	Ⓕ	95	Ⓣ	Ⓕ	135	Ⓣ	Ⓕ	175	Ⓣ	Ⓕ
16	Ⓣ	Ⓕ	56	Ⓣ	Ⓕ	96	Ⓣ	Ⓕ	136	Ⓣ	Ⓕ	176	Ⓣ	Ⓕ
17	Ⓣ	Ⓕ	57	Ⓣ	Ⓕ	97	Ⓣ	Ⓕ	137	Ⓣ	Ⓕ	177	Ⓣ	Ⓕ
18	Ⓣ	Ⓕ	58	Ⓣ	Ⓕ	98	Ⓣ	Ⓕ	138	Ⓣ	Ⓕ	178	Ⓣ	Ⓕ
19	Ⓣ	Ⓕ	59	Ⓣ	Ⓕ	99	Ⓣ	Ⓕ	139	Ⓣ	Ⓕ	179	Ⓣ	Ⓕ
20	Ⓣ	Ⓕ	60	Ⓣ	Ⓕ	100	Ⓣ	Ⓕ	140	Ⓣ	Ⓕ	180	Ⓣ	Ⓕ
21	Ⓣ	Ⓕ	61	Ⓣ	Ⓕ	101	Ⓣ	Ⓕ	141	Ⓣ	Ⓕ			
22	Ⓣ	Ⓕ	62	Ⓣ	Ⓕ	102	Ⓣ	Ⓕ	142	Ⓣ	Ⓕ			
23	Ⓣ	Ⓕ	63	Ⓣ	Ⓕ	103	Ⓣ	Ⓕ	143	Ⓣ	Ⓕ			
24	Ⓣ	Ⓕ	64	Ⓣ	Ⓕ	104	Ⓣ	Ⓕ	144	Ⓣ	Ⓕ			
25	Ⓣ	Ⓕ	65	Ⓣ	Ⓕ	105	Ⓣ	Ⓕ	145	Ⓣ	Ⓕ			
26	Ⓣ	Ⓕ	66	Ⓣ	Ⓕ	106	Ⓣ	Ⓕ	146	Ⓣ	Ⓕ			
27	Ⓣ	Ⓕ	67	Ⓣ	Ⓕ	107	Ⓣ	Ⓕ	147	Ⓣ	Ⓕ			
28	Ⓣ	Ⓕ	68	Ⓣ	Ⓕ	108	Ⓣ	Ⓕ	148	Ⓣ	Ⓕ			
29	Ⓣ	Ⓕ	69	Ⓣ	Ⓕ	109	Ⓣ	Ⓕ	149	Ⓣ	Ⓕ			
30	Ⓣ	Ⓕ	70	Ⓣ	Ⓕ	110	Ⓣ	Ⓕ	150	Ⓣ	Ⓕ			
31	Ⓣ	Ⓕ	71	Ⓣ	Ⓕ	111	Ⓣ	Ⓕ	151	Ⓣ	Ⓕ			
32	Ⓣ	Ⓕ	72	Ⓣ	Ⓕ	112	Ⓣ	Ⓕ	152	Ⓣ	Ⓕ			
33	Ⓣ	Ⓕ	73	Ⓣ	Ⓕ	113	Ⓣ	Ⓕ	153	Ⓣ	Ⓕ			
34	Ⓣ	Ⓕ	74	Ⓣ	Ⓕ	114	Ⓣ	Ⓕ	154	Ⓣ	Ⓕ			
35	Ⓣ	Ⓕ	75	Ⓣ	Ⓕ	115	Ⓣ	Ⓕ	155	Ⓣ	Ⓕ			
36	Ⓣ	Ⓕ	76	Ⓣ	Ⓕ	116	Ⓣ	Ⓕ	156	Ⓣ	Ⓕ			
37	Ⓣ	Ⓕ	77	Ⓣ	Ⓕ	117	Ⓣ	Ⓕ	157	Ⓣ	Ⓕ			
38	Ⓣ	Ⓕ	78	Ⓣ	Ⓕ	118	Ⓣ	Ⓕ	158	Ⓣ	Ⓕ			
39	Ⓣ	Ⓕ	79	Ⓣ	Ⓕ	119	Ⓣ	Ⓕ	159	Ⓣ	Ⓕ			
40	Ⓣ	Ⓕ	80	Ⓣ	Ⓕ	120	Ⓣ	Ⓕ	160	Ⓣ	Ⓕ			

For Office Use

Scale	Raw Score	PS Value
1A		
1B		
2A		
2B		
3A		
3B		
4A		
4B		
5A		
5B		
6A		
6B		
7A		
7B		
8A		
8B		
9A		
9B		
10A		
10B		
11A		
11B		
12A		
12B		
PI		
NI		
CO		

Name _____ Date _____

PS Value

		0	10	20	30	40	50	60	70	80	90	100
Motivating Aims	Enhancing (1A)	•	•	•	•	•	•	•	•	•	•	•
	Preserving (1B)	•	•	•	•	•	•	•	•	•	•	•
	Modifying (2A)	•	•	•	•	•	•	•	•	•	•	•
	Accommodating (2B)	•	•	•	•	•	•	•	•	•	•	•
	Individuating (3A)	•	•	•	•	•	•	•	•	•	•	•
	Nurturing (3B)	•	•	•	•	•	•	•	•	•	•	•
Cognitive Modes	Extraversing (4A)	•	•	•	•	•	•	•	•	•	•	•
	Introversing (4B)	•	•	•	•	•	•	•	•	•	•	•
	Sensing (5A)	•	•	•	•	•	•	•	•	•	•	•
	Intuiting (5B)	•	•	•	•	•	•	•	•	•	•	•
	Thinking (6A)	•	•	•	•	•	•	•	•	•	•	•
	Feeling (6B)	•	•	•	•	•	•	•	•	•	•	•
	Systematizing (7A)	•	•	•	•	•	•	•	•	•	•	•
	Innovating (7B)	•	•	•	•	•	•	•	•	•	•	•
Interpersonal Behaviors	Retiring (8A)	•	•	•	•	•	•	•	•	•	•	•
	Outgoing (8B)	•	•	•	•	•	•	•	•	•	•	•
	Hesitating (9A)	•	•	•	•	•	•	•	•	•	•	•
	Asserting (9B)	•	•	•	•	•	•	•	•	•	•	•
	Dissenting (10A)	•	•	•	•	•	•	•	•	•	•	•
	Conforming (10B)	•	•	•	•	•	•	•	•	•	•	•
	Yielding (11A)	•	•	•	•	•	•	•	•	•	•	•
	Controlling (11B)	•	•	•	•	•	•	•	•	•	•	•
	Complaining (12A)	•	•	•	•	•	•	•	•	•	•	•
	Agreeing (12B)	•	•	•	•	•	•	•	•	•	•	•
Response Indices	Positive Impression (PI)	0	1	2	3	4	5	6	7	8	9	10
	Negative Impression (NI)	0	1	2	3	4	5	6	7	8	9	10
	Consistency (CO)	0	1	2	3	4	5					

Norms (check one)

Adult	College
☐ Female	☐ Female
☐ Male	☐ Male
☐ General	☐ General

Appendix V

Millon Behavioural Medicine Diagnostic Test Booklet

MBMD™

Hand-Scoring Test Booklet

Millon™ Behavioral Medicine Diagnostic

Theodore Millon, PhD, DSc, Michael Antoni, PhD, Carrie Millon, PhD,
Sarah Meagher, MS, and Seth Grossman, MA

Product Number
51931

TEST DIRECTIONS:

The following pages contain statements that describe feelings and attitudes that patients sometimes have. Read each statement carefully and decide if it is true or false for you. Then fill in the Ⓣ or Ⓕ on the separate answer sheet to record your response.

Use a pencil and make a heavy, dark mark when you fill in a circle. If you make a mistake or change your mind, erase the mark completely and then fill in the other circle. *Do not make any marks in this booklet.*

Be as honest and as serious as you can when you are marking your responses.

1. I feel very tense when I think about the day's events.
2. I am not a very spiritual person.
3. I get extremely anxious when I don't know what the doctors are going to do to me.
4. I am a dramatic kind of person.
5. Sometimes I can't remember what medications to take and when to take them.
6. I often get confused about what is happening to me.
7. I can no longer do things I enjoyed doing in the past.
8. I've felt sad much of my life.
9. The idea of being left alone in life really frightens me.
10. Sometimes I take medications that were prescribed for others on the chance that they'll help me.
11. I wish other people were more accepting of me.
12. I can get nasty with people who deserve it.
13. My best years are behind me.
14. I feel jumpy and under strain, but I don't know why.
15. I get great comfort from my religious beliefs.
16. I begin to cry when the smallest things go wrong.
17. I seem to fit in right away with any group of people I meet.
18. I like to follow instructions and do what others expect of me.
19. Most people wouldn't care much if I were sick.
20. Medical instruments really frighten me.
21. Loss of memory has been a big problem for me.
22. I can't move around and do things as well as I could in the past.
23. I want my doctor to review with me the results of all my medical tests.
24. I've found that this society is too hard on people who don't conform.
25. I've felt all alone for a very long time now.
26. I'll stop anyone who tries to boss me around.
27. I would much rather follow someone than be the leader.
28. I get very anxious when I think about my medical problems.
29. I deserve many of the misfortunes I've suffered.
30. I think things will get much worse in the coming months.
31. I can't take care of myself as well as I used to.
32. I try to learn as much as I can about the treatments available for my medical condition.
33. Faith and prayer always get me through my troubles.
34. I have a lot of confidence in myself.
35. I'm trying to be as open as I can in my responses to these questions.
36. I protect myself by not letting people know much about my life.
37. I guess I've always been a fearful and inhibited person.
38. If you don't have something good to say about yourself, you should keep quiet.
39. I would do anything to stop the pain I feel.
40. I seem to need a lot of advice in order to get things done.

Please go to the next page

41. If I have to go through another medical procedure, I think I'll just go crazy.
42. My health seems to be failing faster than that of most people my age.
43. Life will never be the same again for me.
44. No matter what, seeing a doctor is reassuring.
45. I rarely find the time to exercise.
46. I feel so jittery and restless that I'm worn out at night.
47. I've always preferred to have a quiet and inactive life.
48. I have a habit of making my problems sound worse than they really are.
49. I have been having serious thoughts about suicide.
50. I like to arrange things down to the last detail.
51. There's little emotional support within my family.
52. I have always had a talent for being successful.
53. I have told lies to my family to conceal my use of drugs.
54. Very few people appreciate just how hard my life really is.
55. I seem to be losing my ability to concentrate.
56. Answering questions like these helps me take a good honest look at things in my life.
57. I watch out for people trying to cheat me.
58. The pain I'm in has made my life feel very hopeless.
59. In this world you either push or get shoved.
60. I'm very erratic, changing my feelings all the time.
61. When people are bossy, I usually do the opposite of what they want.
62. I've had nightmares about medical procedures I may have to endure.
63. I worry a lot that the people I depend on will leave me.
64. I'm my own worst enemy.
65. I sometimes exaggerate how poorly I am feeling.
66. For some unknown reason, I suddenly get very panicky.
67. My emotions don't seem to be as strong as other people's.
68. It makes me very uncomfortable when other people know about my problems.
69. Physical pain is a big part of my life.
70. I am constantly worried about my health.
71. It is good to have a routine for doing things in order to avoid mistakes.
72. There is someone close to me who truly understands my feelings.
73. Many people respect and envy me.
74. Taking drugs has been a regular part of my social life.
75. I believe something is wrong with my head.
76. Most people in my life eventually disappoint me.
77. I feel particularly resentful when I am refused medical benefits I know I am entitled to.
78. It's all right to bend the law as long as you don't break it.
79. I never let anyone get the better of me.
80. I know from the past that good things don't last.

Please go to the next page

81. I can handle the worst medical news about myself, no matter how upsetting it may be.
82. I am afraid that I may suddenly die from an illness.
83. I am quickly losing hope that I will ever regain my health.
84. I make sure that I'm on time for all my doctor's appointments.
85. Pain makes it very difficult for me to work now.
86. I have found very few things in life to be pleasurable.
87. I have many very good and close friends.
88. I always finish my work before I take time out for leisure.
89. I have friends who will listen to any problem I have.
90. Everything I try comes easily to me.
91. I'm making myself seem healthier in my responses here than I really am.
92. My life has always gone from bad to worse.
93. I think it's best not to trust anyone.
94. Pain is the worst part of my medical condition.
95. I often resent doing things that others expect of me.
96. I am mistreated most by close friends and relatives.
97. I quickly consult my doctor whenever I have new symptoms.
98. I'm on edge a lot lately.
99. I am never alone as long as God is with me.
100. I think I'm a very sociable and outgoing person.
101. It is always best to follow the rules that those in authority have made.
102. A lot of my answers on this test have been affected by my current bad mood.
103. I sometimes take medications that are prescribed for other people.
104. I often set myself up to fail.
105. I feel guilty most of the time.
106. I flew across the Atlantic more than 30 times last year.
107. My feelings toward my relatives often swing back and forth from love to hate.
108. I want my doctors to be as detailed as possible in telling me about my medical problems.
109. I don't think I'll live as long as I should.
110. I make my life worse than it has to be.
111. I smoke about a pack of cigarettes a day.
112. I've never had as much interest in sex as most people my age.
113. I'm too embarrassed to admit my problems as frankly as I should.
114. I can charm people into doing almost anything I want.
115. I've been overweight ever since I was a child.
116. If I don't get relief from medicine, I may increase the dosage on my own.
117. In the past year, I've really gone downhill mentally.
118. I think I am making my life look worse than it really is by my responses here.
119. I spend much of my time brooding about things.
120. Too many rules get in the way of people doing what they want to do.

Please go to the next page

121. No one needs to know my business.
122. I've always felt that most people think poorly of me.
123. I'm considered a tough and unsentimental person.
124. I was on the front cover of several magazines recently.
125. I get very annoyed when others put pressure on me.
126. My body is constantly giving me worrisome signals.
127. It is difficult for me to get through the day without a few drinks.
128. I never put off seeing the doctor if I feel I need to.
129. Being in touch with my spiritual self helps me deal with life's burdens.
130. I often feel sad and unloved.
131. I start feeling crazy when medical problems turn out badly for me.
132. I am holding back when I respond to many of these statements.
133. I feel entitled to all my sick days each year.
134. I'd rather not know the details of an illness I might have.
135. I get very irritable if I haven't had a cup of coffee for a few hours.
136. The quality of my life has gotten much worse because of my illness.
137. I rarely feel a sense of joy these days.
138. I usually do what I want without worrying about how it affects others.
139. I'm a yo-yo dieter; my weight goes up and down.
140. My head often hurts so much that I need to take time off from work.
141. This is a very lonely world.
142. I've tried to quit smoking many times, but I always start again.
143. I would change my lifestyle on my doctor's advice.
144. Without God in my life, I could never get through a serious illness.
145. My pain is on my mind constantly.
146. I always overeat when I'm depressed or under stress.
147. My future looks like it will be full of problems and pain.
148. It's okay to take advantage of gray areas in the law.
149. I've tried exercise programs, but I just can't seem to stick with them.
150. I'm unable to organize my life the way I want.
151. Members of my family have complained recently about my drinking.
152. I really don't understand human feelings like others do.
153. I need plenty of caffeine to get me through the day.
154. I almost always put other people's needs above my own.
155. I often feel overwhelmed by minor responsibilities.
156. I've lost interest in things that I used to find pleasurable.
157. I now need to follow routines so that I don't get confused.
158. My medical condition has made daily tasks much more difficult.
159. I know I should exercise, but I just can't get started.
160. I cannot count on anyone to support me during times of illness.

Please go to the next page

161. I feel very depressed.
162. I am a very emotional person.
163. I like to flirt with members of the opposite sex.
164. I get irritable if I go too long without a cigarette.
165. I have no deep religious beliefs.

Appendix VI

Millon Behavioural Medicine Diagnostic
Answer Sheet

MILLON BEHAVIORAL MEDICINE DIAGNOSTIC

Hand-Scoring Answer Sheet

MBMD™

Millon™ Behavioral Medicine Diagnostic

by Theodore Millon, PhD, DSc, Michael Antoni, PhD, Carrie Millon, PhD, Sarah Meagher, MS, and Seth Grossman, MA

NAME OR IDENTIFICATION NUMBER

TEST DATE BIRTH DATE GENDER

RACE/ETHNICITY (Optional–for research use only)

1 (T) (F)	31 (T) (F)	61 (T) (F)	91 (T) (F)	121 (T) (F)	151 (T) (F)
2 (T) (F)	32 (T) (F)	62 (T) (F)	92 (T) (F)	122 (T) (F)	152 (T) (F)
3 (T) (F)	33 (T) (F)	63 (T) (F)	93 (T) (F)	123 (T) (F)	153 (T) (F)
4 (T) (F)	34 (T) (F)	64 (T) (F)	94 (T) (F)	124 (T) (F)	154 (T) (F)
5 (T) (F)	35 (T) (F)	65 (T) (F)	95 (T) (F)	125 (T) (F)	155 (T) (F)
6 (T) (F)	36 (T) (F)	66 (T) (F)	96 (T) (F)	126 (T) (F)	156 (T) (F)
7 (T) (F)	37 (T) (F)	67 (T) (F)	97 (T) (F)	127 (T) (F)	157 (T) (F)
8 (T) (F)	38 (T) (F)	68 (T) (F)	98 (T) (F)	128 (T) (F)	158 (T) (F)
9 (T) (F)	39 (T) (F)	69 (T) (F)	99 (T) (F)	129 (T) (F)	159 (T) (F)
10 (T) (F)	40 (T) (F)	70 (T) (F)	100 (T) (F)	130 (T) (F)	160 (T) (F)
11 (T) (F)	41 (T) (F)	71 (T) (F)	101 (T) (F)	131 (T) (F)	161 (T) (F)
12 (T) (F)	42 (T) (F)	72 (T) (F)	102 (T) (F)	132 (T) (F)	162 (T) (F)
13 (T) (F)	43 (T) (F)	73 (T) (F)	103 (T) (F)	133 (T) (F)	163 (T) (F)
14 (T) (F)	44 (T) (F)	74 (T) (F)	104 (T) (F)	134 (T) (F)	164 (T) (F)
15 (T) (F)	45 (T) (F)	75 (T) (F)	105 (T) (F)	135 (T) (F)	165 (T) (F)
16 (T) (F)	46 (T) (F)	76 (T) (F)	106 (T) (F)	136 (T) (F)	
17 (T) (F)	47 (T) (F)	77 (T) (F)	107 (T) (F)	137 (T) (F)	
18 (T) (F)	48 (T) (F)	78 (T) (F)	108 (T) (F)	138 (T) (F)	
19 (T) (F)	49 (T) (F)	79 (T) (F)	109 (T) (F)	139 (T) (F)	
20 (T) (F)	50 (T) (F)	80 (T) (F)	110 (T) (F)	140 (T) (F)	
21 (T) (F)	51 (T) (F)	81 (T) (F)	111 (T) (F)	141 (T) (F)	
22 (T) (F)	52 (T) (F)	82 (T) (F)	112 (T) (F)	142 (T) (F)	
23 (T) (F)	53 (T) (F)	83 (T) (F)	113 (T) (F)	143 (T) (F)	
24 (T) (F)	54 (T) (F)	84 (T) (F)	114 (T) (F)	144 (T) (F)	
25 (T) (F)	55 (T) (F)	85 (T) (F)	115 (T) (F)	145 (T) (F)	
26 (T) (F)	56 (T) (F)	86 (T) (F)	116 (T) (F)	146 (T) (F)	
27 (T) (F)	57 (T) (F)	87 (T) (F)	117 (T) (F)	147 (T) (F)	
28 (T) (F)	58 (T) (F)	88 (T) (F)	118 (T) (F)	148 (T) (F)	
29 (T) (F)	59 (T) (F)	89 (T) (F)	119 (T) (F)	149 (T) (F)	
30 (T) (F)	60 (T) (F)	90 (T) (F)	120 (T) (F)	150 (T) (F)	

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Appendix VII

Definitions of MIPS Scales

The 24 MIPS scales are organised into three major areas: Motivating Aims, Cognitive Modes, and Interpersonal Behaviours. A brief definition of each of the 24 MIPS scales follows:

Motivating Aims

Enhancing Persons scoring high on this scale tend to look for the bright side of life, are optimistic about future possibilities, find it easy to enjoy themselves, and face the ups and downs of life with equanimity.

Preserving Persons scoring high on this scale focus on and intensify the problems of life. Perceiving the past as having been personally troubling, they always seem to be waiting for something else to go wrong, and feel that things are likely to go from bad to worse. They are easily upset by minor concerns and disappointments.

Modifying Persons scoring high on this scale take charge of their lives and make things happen rather than wait for them to occur. They are busily involved in modifying their environments and arranging events to suit their needs and desires.

Accommodating Persons scoring high on this scale undertake little to shape or alter their lives. They react to the passing scene, accommodating to circumstances created by others; they seem acquiescent, are unable to rouse themselves, lack initiative, and do little to generate the outcomes they desire.

Individuating Persons scoring highly on this scale are oriented to actualise their own needs and wishes, that is, they seek to fulfil themselves first, worry little about the impact of their behaviour on others, and tend to be both independent and egocentric.

Nurturing Persons scoring high on this scale are motivated to meet the needs of others first; to attend to other people's welfare and desires at the expense of themselves. They are seen as nurturant and protective taking care of others before taking care of themselves.

Cognitive Modes

Extraversing High scorers turn to others to find stimulation and encouragement. They draw upon friends and colleagues for ideas and guidance, inspiration and energy, as well as garnering assurances of self-worth from them and taking comfort in their presence.

Introversing High scorers prefer to use their own thoughts and feelings as resources, gaining inspiration and stimulation primarily from themselves rather than from others. By contrast with extraverts, introverts experience greater serenity and comfort by distancing themselves from external sources, preferring to heed the prompting that comes from within.

Sensing High scorers gather their knowledge from the tangible and concrete, trusting direct experience and observable phenomena over the use of inference and abstraction. The practical and 'real', the literal and factual are what give these individuals comfort and confidence.

Intuiting High scorers prefer the symbolic and unknown to the concrete and observable. They are open to the intangibles of life and are inclined to seek out and enjoy the more mysterious experiences and speculative sources of knowledge.

Thinking High scorers prefer to process the knowledge they have by means of logic and analytical reasoning. Decisions are based on cool, impersonal, and 'objective' judgements, rather than on subjective emotions.

Feeling High scorers form their judgements by heeding their own affective responses to circumstances, by evaluating subjectively the impact of their actions upon those involved, and by following their personal values and goals.

Systematising High scorers are very organised and predictable in their approach to life's experiences. They transform new knowledge in line with what is known and are careful, if not perfectionistic, in arranging even minor details. As a result, others see them as orderly, conscientious, and efficient.

Innovating High scorers are inclined to be creative and to take risks, ready to alter and recast whatever they come upon. They seem discontented with the routine and predictable; spontaneously

modifying what is given by following their hunches and seeking to effect novel, unanticipated consequences.

Interpersonal Behaviours

Retiring Persons scoring high on this scale are characterised by their lack of affect and their social indifference. They tend to be quiet, passive, and uninvolved; they may be viewed by others as quiet and colourless, unable to make friends, as well as apathetically disengaged.

Outgoing High scorers seek social stimulation, excitement and attention. They often react dramatically to situations around them, but typically, they lose interest very quickly. Colourful and charming socialites, they can also be demanding and manipulative.

Hesitating High scorers are usually shy, timid and nervous in social situations, strongly wanting to be liked and accepted, yet often fearing rejection. At the same time they are sensitive and emotionally responsive, they are mistrusting, lonely, and isolated.

Asserting High scorers tend to feel that they are more important and gifted than the people around them. They are often ambitious and egocentric, self-assured and outspoken. Others may see them as arrogant and inconsiderate.

Dissenting High scorers tend to act out in an independent and non-conforming manner. They often resist following traditional standards, displaying an audaciousness that may be seen either as reckless or as spirited and enterprising.

Conforming High scorers are likely to upstanding and self-controlled. They relate to authority in a respectful and co-operative manner, tend to behave in a formal and proper manner in social situations, and are unlikely to be self-expressive or to act spontaneously.

Yielding High scorers are their own worst enemies: They are accustomed to suffering rather than pleasure, are submissive, and tend to act in self-demeaning ways. Their behaviour renders ineffective the efforts of others to assist them, and causes the yielders to bypass opportunities for rewards and to fail repeatedly to achieve despite possessing abilities to do so.

Controlling High scorers are forceful and often domineering and socially aggressive. They tend to see themselves as fearless and competitive. To them, warmth and gentleness are signs of weakness, which they avoid by being strong-willed and ambitious.

Complaining High scorers are characterised by their tendency to be passive-aggressive, sullen, and generally dissatisfied. Their moods and behaviour are highly changeable: At times, they relate to others in a sociable and friendly manner: on other occasions, they are irritable and hostile, expressing the belief that they are misunderstood and unappreciated.

Agreeing High scorers tend to be highly likeable socially, often relating to others in an amenable manner. They form strong loyalties and attachments to others. They cover any negative feelings, however, especially when these feelings may be viewed as objectionable by the people they wish to please.

Appendix VIII

Definition of MBMD Scales

The MBMD is comprised f seven domains. Each domain contains a series of scales. The domains are: Response Patterns, Negative Health Habits, Psychiatric Indications, Coping Styles, Stress Moderators, and Treatment Prognostics. A brief description of those scales used in the research follows:

Response Patterns:

Validity The validity indicator is composed of two highly improbable items (Items 106 & 124 – refer to Appendix). Endorsements on the validity indicator may indicate inadequate reading skills, confusion, or random responding. In this research no respondents endorsed either item.

Disclosure The scale is designed to determine whether the patient is inclined to be overly frank or self-revealing. No respondents obtained scores that may have signified a troublesome level of disclosure.

Desirability This scale identifies the degree to which the respondent's results may have been affected by his/her desire to appear socially attractive, morally virtuous, or emotionally well composed. High scores indicate a greater likelihood that the respondent is concealing important psychological stressors or behavioural problems. No respondents obtained any suggestive scores on this scale.

Debasement This scale assesses the respondent's tendency to present many minor and major symptoms, sensations, and experiences in his/her communication with the healthcare provider. The scale reflects tendencies that are the opposite of those detected by the Desirability scale. High scorers are inclined to devalue themselves by reporting more troublesome emotions or medical problems than are likely to be uncovered in an objective review. No respondents obtained any significant scores on this scale.

Negative Health Habits

The indicators included in this domain cover lifestyle behaviours that have been shown to have the strongest contribution to the widest variety of health outcomes: Alcohol, drugs, Eating, Caffeine, Inactivity, and Smoking.

Psychiatric Indications

Anxiety-Tension High scorers may suffer from numerous somatic disorders, especially those associated with the cardiovascular and digestive systems.

Depression High scorers tend to interpret life as a series of troubles and misfortunes and are likely to intensify the discomfort of their real physical and psychological problems.

Cognitive Dysfunction This scale assesses the capacity to recall past experiences, to think abstractly, and to represent events and interrelate and process them symbolically.

Emotional Lability This scale assesses the experience of intense endogenous moods and respondents may exhibit recurring periods of dejection, and apathy, often interspersed with spells of anger, anxiety, or euphoria. They are typified by dysregulation of their affect and instability in their moods, perhaps at one extreme, manifested in repetitive suicidal thoughts or self-harm.

Guardedness This scale aims to identify medical patients who display mistrust and an edgy defensiveness against those they see as hostile and deceptive. They may exhibit irritability and suspiciousness, and they often provoke annoyance, if not exasperation, on the part of healthcare providers.

Coping Styles

Introversive High scorers tend to be rather colourless, emotionally subdued, and quiet. Typically, they lack energy, are communicatively vague, and are difficult to pin down regarding their symptoms. Some may have become withdrawn as a way of coping with a chronic illness.

Inhibited High scorers tend to be shy, ill at ease, and hesitant with others. They may be sensitive and are often concerned that others may do them harm. Because they may fear that others take advantage of them, they may try to keep their physical discomfort to themselves. Their isolation may also stem from a loss of self-esteem consequent to persistent illness. Despite their hesitation, they do want understanding and attention. With a sympathetic clinical attitude, they can become quite co-operative.

Dejected High scorers are inclined to be persistently and characteristically disheartened, unable to experience the pleasures or joys of life. They are easily disposed to give up trying to work through their emotional or physical problems. Their disconsolate and somewhat hopeless orientation will call for greater effort than usual from healthcare staff.

Co-operative High scorers tend to be eager to attach themselves to a supportive healthcare professional, and will follow medical advice closely. However, they may not take the initiative to seek treatment and will need to be told exactly what to do. Healthcare personnel may have to probe carefully and ask explicit questions to get the information they need. They become overly dependent on their carers.

Nonconforming High scorers tend to be somewhat unconventional if not arbitrary and occasionally inconsiderate in their manner. They are somewhat sceptical about the motives of others, and they tend to act insensitively and impulsively at times. Healthcare professionals should assure them that they are there to help them solve their physical problems in a professional way.

Forceful High scorers tend to be rather domineering and tough-minded. The healthcare team should try not to feel intimidated or provoked by these individuals. A straightforward approach is most effective with these patients. They may have a tendency to be mistrustful, and may not follow treatment regimens well. It will be necessary for the healthcare team to exert extra effort to encourage them to comply.

Respectful High scorers are likely to be responsible, conforming, and co-operative. They keep their feelings to themselves and try to appear controlled, diligent, and serious-minded. These patients usually take their medication and follow therapeutic recommendations. However, they are very likely to hide their symptoms, and they may resist disclosing their problems. They do not like to be seen in the patient role because it signifies weakness and inefficiency to them.

Oppositional High scorers are often unpredictable and difficult. They may be erratic in following a treatment plan – overmedicating and under medicating without consulting their attending healthcare worker. They often seem displeased and dissatisfied with their physical and psychological state. At times, they will complain about their treatment, but this may quickly switch to expressions of regret and contrition. They often have mood changes for no obvious reason, and rapport may be easy on some days but difficult on others.

Denigrated High scorers habitually focus on the most troublesome aspects of their lives, behaving as if they deserve to suffer. They may feel that they deserve the infirmities and ailments they experience, and they may actively and repetitively recall past troubles and afflictions.

Stress Moderators

Illness Apprehension vs. Illness Acceptance The Illness Apprehension scale reflects patients' focus on and awareness of changes in their bodies such as tension/relaxation and arousal/fatigue. They may either have an ability to monitor and report significant changes in symptoms, or attend to less important sensations in a way that they ruminate excessively about their medical state and medical services. Illness Acceptance reflects the behavioural assets of self-possession and imperturbability.

Social Isolation vs. Social Support This scale assesses respondents' perceptions of the social support in their lives. High scorers are more likely to suffer physical and psychological ailments than low scorers. Poor adjustment to hospitalisation is also common.

Future Pessimism vs. Future Optimism This scale is designed to assess patients' outlook toward their future health status. This patient characteristic may influence a number of medical outcomes including adherence to and confidence in medical regimens, emotional reactions to diagnostic test results, and probably the actual physical course of disease. A high score may reflect a patient's response to his/her current medical problems rather than a lifelong tendency to be pessimistic.

Treatment Prognostics

Interventional Fragility vs. Interventional Resilience The Interventional Fragility scale predicts whether patients will be able to adjust emotionally to the demands of physically and psychologically stressful medical protocols. This is most useful in a medical/surgical context.

Medication Abuse vs. Medication Conscientiousness This scale predicts the likelihood that patients will have problems with or will misuse prescribed medication. This might take the form of changing dosages, combining medications inappropriately, or using outdated prescriptions. These behaviours can be dangerous and should be identified at the earliest point in the treatment process.

Information Discomfort vs. Information Receptivity This scale assesses patients' lack of receptivity to specific details about diagnostic, prognostic, and treatment procedures and outcomes.

Some patients want to know as much as they can about their medical condition and prognosis. Others do not, sometimes to the point of not wanting to know the name of their disorder much less its character or prognosis.

Problematic Compliance vs. Optimal Compliance A major problem for healthcare professionals is patients who either inadvertently or intentionally resist following medical recommendations. This scale assesses compliance problems and identifies the disinclination to follow home-care advice, to adhere to medication instruction, and to be and keep on time for appointments.

Management Guides

The Management Guides domain includes two summary scales: Adjustment Difficulties and Psych Referral. These scales integrate and summarise a patient's major problem areas. They were not consulted within this research.

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Inhibited High scorers tend to be shy, ill at ease, and hesitant with others. They may be sensitive and are often concerned that others may do them harm. Because they may fear that others take advantage of them, they may try to keep their physical discomfort to themselves. Their isolation may also stem from a loss of self-esteem consequent to persistent illness. Despite their hesitation, they do want understanding and attention. With a sympathetic clinical attitude, they can become quite co-operative.

Dejected High scorers are inclined to be persistently and characteristically disheartened, unable to experience the pleasures or joys of life. They are easily disposed to give up trying to work through their emotional or physical problems. Their disconsolate and somewhat hopeless orientation will call for greater effort than usual from healthcare staff.

Co-operative High scorers tend to be eager to attach themselves to a supportive healthcare professional, and will follow medical advice closely. However, they may not take the initiative to seek treatment and will need to be told exactly what to do. Healthcare personnel may have to probe carefully and ask explicit questions to get the information they need. They become overly dependent on their carers.

Nonconforming High scorers tend to be somewhat unconventional if not arbitrary and occasionally inconsiderate in their manner. They are somewhat sceptical about the motives of others, and they tend to act insensitively and impulsively at times. Healthcare professionals should assure them that they are there to help them solve their physical problems in a professional way.

Forceful High scorers tend to be rather domineering and tough-minded. The healthcare team should try not to feel intimidated or provoked by these individuals. A straightforward approach is most effective with these patients. They may have a tendency to be mistrustful, and may not follow treatment regimens well. It will be necessary for the healthcare team to exert extra effort to encourage them to comply.

Respectful High scorers are likely to be responsible, conforming, and co-operative. They keep their feelings to themselves and try to appear controlled, diligent, and serious-minded. These patients usually take their medication and follow therapeutic recommendations. However, they are very likely to hide their symptoms, and they may resist disclosing their problems. They do not like to be seen in the patient role because it signifies weakness and inefficiency to them.

Oppositional High scorers are often unpredictable and difficult. They may be erratic in following a treatment plan – overmedicating and under medicating without consulting their attending healthcare worker. They often seem displeased and dissatisfied with their physical and psychological state. At times, they will complain about their treatment, but this may quickly switch to expressions of regret and contrition. They often have mood changes for no obvious reason, and rapport may be easy on some days but difficult on others.

Denigrated High scorers habitually focus on the most troublesome aspects of their lives, behaving as if they deserve to suffer. They may feel that they deserve the infirmities and ailments they experience, and they may actively and repetitively recall past troubles and afflictions.

Stress Moderators

Illness Apprehension vs. Illness Acceptance The Illness Apprehension scale reflects patients' focus on and awareness of changes in their bodies such as tension/relaxation and arousal/fatigue. They may either have an ability to monitor and report significant changes in symptoms, or attend to less important sensations in a way that they ruminate excessively about their medical state and medical services. Illness Acceptance reflects the behavioural assets of self-possession and imperturbability.

Social Isolation vs. Social Support This scale assesses respondents' perceptions of the social support in their lives. High scorers are more likely to suffer physical and psychological ailments than low scorers. Poor adjustment to hospitalisation is also common.

Future Pessimism vs. Future Optimism This scale is designed to assess patients' outlook toward their future health status. This patient characteristic may influence a number of medical outcomes including adherence to and confidence in medical regimens, emotional reactions to diagnostic test results, and probably the actual physical course of disease. A high score may reflect a patient's response to his/her current medical problems rather than a lifelong tendency to be pessimistic.

Treatment Prognostics

Interventional Fragility vs. Interventional Resilience The Interventional Fragility scale predicts whether patients will be able to adjust emotionally to the demands of physically and psychologically stressful medical protocols. This is most useful in a medical/surgical context.

Medication Abuse vs. Medication Conscientiousness This scale predicts the likelihood that patients will have problems with or will misuse prescribed medication. This might take the form of changing dosages, combining medications inappropriately, or using outdated prescriptions. These behaviours can be dangerous and should be identified at the earliest point in the treatment process.

Information Discomfort vs. Information Receptivity This scale assesses patients' lack of receptivity to specific details about diagnostic, prognostic, and treatment procedures and outcomes.

Some patients want to know as much as they can about their medical condition and prognosis. Others do not, sometimes to the point of not wanting to know the name of their disorder much less its character or prognosis.

Problematic Compliance vs. Optimal Compliance A major problem for healthcare professionals is patients who either inadvertently or intentionally resist following medical recommendations. This scale assesses compliance problems and identifies the disinclination to follow home-care advice, to adhere to medication instruction, and to be and keep on time for appointments.

Management Guides

The Management Guides domain includes two summary scales: Adjustment Difficulties and Psych Referral. These scales integrate and summarise a patient's major problem areas. They were not consulted within this research.